Automated Patch Clamp User Meeting 2017

June 9th 2017
Cambridge, MA
Key Note Speakers

**Dr. Chris Miller, Professor** Biochemistry Brandeis University: *A Weird Ion Channel for a Very Weird Ion*

**Dr. Owen McManus, CTO** Q-State Biosciences Inc.: *Phenotypic Assays of Neuronal Function to support Drug Discovery*

Dr. Owen McManus has extensive experience in ion channel drug discovery and technology development. He received his Ph.D. in Physiology from the University of Utah in 1983 and went on to complete his Postdoc in the lab of Dr. Karl Magleby, focusing on Physiology & Biophysics. He spent more than twenty years devoted to ion channel drug discovery efforts in pharmaceutical and academic settings for a range of therapeutic areas (pain, glaucoma, diabetes, asthma, hypertension, and immunosuppression) leading to selection of several preclinical and clinical candidate compounds. He has contributed in several areas in basic drug discovery including target identification and validation, assay and technology development, lead identification and optimization, and early clinical studies. He has worked on technology and instrument development in support of drug discovery leading to release of commercial instruments and reagents. His recent work focuses on developing and utilizing optical technologies to enable improved disease models, patient stratification and drug discovery.

Dr. Chris Miller studies the molecular mechanisms by which ion channels and membrane transport proteins work. He received his Ph.D. in Molecular Biology from the University of Pennsylvania in 1974 and went on to complete his Postdoc in Biochemistry at Cornell University in 1976. Dr. Miller pioneered techniques to record the activity of ion channels reconstituted into planar phospholipid membranes allowing the study of the single-molecule behavior of these proteins in a biochemically defined system. His research career has spanned fundamental changes in the ways these membrane proteins can be studied, from cellular patch-recording and membrane reconstitution, to recombinant DNA manipulation, to high-level expression, and x-ray crystallography. He has endeavored to stay current with all these developments, bringing them to bear on questions of membrane transport mechanism.
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Morning Session Agenda

8:15 – 9:00 AM
Arrival & Breakfast
Charles View Ballroom 16th Floor
Poster Set Up
Foyer Area 16th Floor

9:00 – 9:15 AM
Rodolfo Haedo, Senior Vice President Nanion Technologies:
Welcome & Introduction

9:15 – 10:00 AM
– Keynote –
Dr. Chris Miller, Professor Biochemistry Brandeis University:
A Weird Ion Channel for a Very Weird Ion.

10:00 – 10:30 AM
Dr. Alfred George, Professor & Chair Department of Pharmacology Northwestern University:
Automated Electrophysiology of iPSC-derived Cardiomyocytes.

10:30 – 11:00 AM
Dr. Tim Strassmaier, Senior Scientist Nanion Technologies:
Pursuit of TRP channel targets with the SyncroPatch 384PE.

11:00 – 11:15 AM
Poster & Coffee Break
Foyer Area 16th Floor

11:15 AM – 11:45 AM
Andrew Allen & David Baez, Broad Institute:
The Agony and Ecstasy: Characterization of Disease-Related Ion Channel Variants using the SyncroPatch 384PE.

11:45 AM – 12:15 PM
Dr. Bjorn Knollmann, Director Vanderbilt Center for Arrhythmia Research:
Modeling Heart Disease with human iPSC-derived Cardiomyocytes - First Experiences with CardioExcyte 96.

12:15 – 2:00 PM
Lunch
16th floor
Afternoon Session Agenda

1:15 – 2:00 PM  
**– Keynote –**  
**Dr. Owen McManus, CTO** Q-State Biosciences Inc.:  
*Phenotypic Assays of Neuronal Function to support Drug Discovery.*

2:00 - 2:30 PM  
**Dr. Maria Barthmes, Product Manager** Nanion Technologies:  
*Targeting Transporters: High Throughput Screening and Characterization of Membrane Transporters and Pumps with the SURFElD R 96SE.*

2:30 - 3:00 PM  
**Dr. Matt Fuller, Senior Scientist** Icagen, Inc.:  
*Advancing Early Drug Discovery with the SyncroPatch 384PE at Icagen.*

3:00 - 3:30 PM  
**Dr. Greg Kaczorowski, CEO** Kanalis Consulting, L.L.C.:  
*Lessons Learned in Drugging Ion Channels from Prosecuting the Novel ROMK Target.*

3:30 - 4:00 PM  
**Poster and Coffee break**  
Foyer Area 16th Floor

4:00 - 4:30 PM  
**Dr. Srinivasan Venkatachalan, Assist Principal Scientist** Chromocell Corporation:  
*Ion Channel Therapeutic Discovery and Development Effort at Chromocell Corporation using Patchliner.*

4:30 - 5:00 PM  
**Dr. Carlos Vanoye, Research Assoc. Professor** Northwestern University:  
*High Throughput Functional Analysis of Ion Channel Gene Variants.*

5:30  
**Reception and Dinner**  
Foyer Area 16th Floor
Poster Session Abstracts

1. **Next level toxicity screening: From single channel to overall cell behavior**

Conrad Weichbrodt¹, Mohamed Kreir¹, Matthias Beckler¹, Alison Obergrussberger¹, Ilka Rinke¹, Michael George¹, Sonja Stoelze-Feix¹, Andrea Brüggemann¹, Niels Fertig¹

¹Nanion Technologies GmbH, Munich, Germany

Many lead compounds fail in the late stages of the drug development process mainly by inflicting drug induced injury on liver, heart or other organs. Therefore, devices for detecting possible cell toxicity in early stages of the development process are highly desired. Ion channels represent an especially important class of drug targets for in vitro pharmacological profiling. High throughput screening (HTS) assays such as automated electrophysiological patch clamp and impedance based assays allow for the determination of drug effects on a wholecell level whereas artificial bilayers provide a robust environment for the assessment of single ion channel molecules. We here present the CardioExcyte 96, a system providing a combination of Electric Impedance Spectroscopy (EIS) as well as Electric Field Potential (EFP) readout for a network of diverse cells like iPS cardiomyocytes or hepatocyte-like cells which is exemplified by toxicity effects utilizing reference compounds such as Dofetilide (on iPS cardiomyocytes) or Paracetamol (on hepatocyte-like cells). Furthermore we present the temperature dependent activation or deactivation of different Transient Receptor Potential (TRP) channels by means of planar patch clamping on our HTS platforms Patchliner and SyncroPatch 384PE as well as with highest resolution on a single channel level on our recently introduced Orbit mini setup.

2. **A new analysis pipeline to improve assessment of cardiac liability in high throughput electrophysiology screens with routine MoA detection for slow onset compounds**

Stephan Steigele¹, Ana L. Teixeira², Martin Ginkel¹, Verity A Talbot², Lisa J McWilliams², Matt Bridgland-Taylor², Stephan Heyse¹

¹Genedata AG, Basel, Switzerland, ²AstraZeneca, Cambridge

Automated patch clamp screens generate highly valuable information for drug research programs. In safety pharmacology in particular, early testing is nowadays considered essential to manage the risk of late failure and patient health. Thus, more predictive and affordable screens need to be introduced to increase both specificity and throughput e.g. for cardiovascular liability detection and resolution.

At AstraZeneca, we have implemented the Nanion SyncroPatch 384PE electrophysiology platform in standard 384-well plate format, which delivers higher throughput measurements for hERG and other key cardiac ion channels at dramatically reduced consumable costs and experiment time, whilst capturing full channel response kinetics. Jointly with Genedata
we developed a pipeline for processing and analyzing this complex data. This pipeline reads binary raw data directly from the SyncroPatch 384PE instrument into Genedata Screener®, then assigns and integrates the sweep recordings from cumulative compound addition series, and finally subjects the recordings to scientist review that uses powerful filtering and masking based on quality control measurements. We further developed two methods: The first to normalize the cumulative curve recordings, which are compensated for signal variation using time-match control, and the second to automatically detect “slow onset” compounds using a sigmoidal fit model per concentration step. Because of their slow onset, these compounds were previously potentially underestimated, but are now flagged.

This investment in a next-generation automated electrophysiology platform and an appropriate automated data processing pipeline is resulting in more predictive and affordable safety screens at high scalability and rapid turnover for discovery projects across AstraZeneca.

3. Preclinical Cytotoxicity Investigations in Stem Cells for Primary and Secondary Assays with an “All Inclusive” Approach

Corina T. Bot2, Sonja Stölzle-Feix1, Nadine Becker1, Ulrich Thomas1, Krisztina Juhasz1, Leo Doerr1, Matthias Beckler1, Claudia Haarmann1, Alison Obergrussberger1, Susanne M. Rehnelt3, Tobias Bruegmann3, Philipp Sasse3, J-F. Rolland4,5, R. Rizzetto4,5, V. Agus4,5, L. Redaelli4,5, Rodolfo J. Haedo2, Andrea Brüggemann1, Michael George1, Niels Fertig1

1Nanion Technologies GmbH, Gabrielenstr. 9, 80636 Munich, Germany; 2Nanion Technologies Inc. 1 Naylon Place, Livingston, NJ, 07039, USA; 3Inst. für Physiologie I, Univ. Bonn, Life and Brain Center, Bonn, Germany; 4Axxam S.p.A., Openzone - via Meucci 3, 20091 Bresso - Milan, Italy; 5OPTEL Consortium funded by EuroTransBio Initiative

Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have recently proven to recapitulate key features of human cardiac electrophysiology in vitro. Chip-based approaches allow parallel patch clamp recordings without compromising data quality or technical sophistication. Voltage and current clamp recordings on Nanion’s SyncroPatch 384 patch clamp platform are presented. In addition to patch-clamping experiments, we present hybrid impedance (cell contractility) with MEA-like extracellular field potential (EFP) recordings. Experiments were complemented with optical stimulation of monolayers of hiPSC-CMs expressing the light-gated cation channel Channelrhodopsin2. This approach allows frequency-dependent drug screening and detection of potential side effects on Na+, Ca2+ and repolarizing K+ channels. Furthermore, investigations of potential breaks in excitation-contraction coupling can accompany ion channel screening with the final aim to enable a reliable automatized cardiac toxicity screening platform.
4. **Nanion CardioExcyte 96: the Workhorse for iPSC Cardiomyocyte Quality Control that Allows for Mechanistic Insights into Contractility and Electrophysiology by SOL Optical Stimulation**

Chris Fleming¹, Corina Bot², Greg Luerman¹, Ralf Kettenhofen¹, Anika Duenbostell¹, Heribert Bohlen¹

¹Axiogenesis AG, Cologne, Germany; ²Nanion Technologies Inc., Livingston, NJ, USA

Monolayers of human iPSC-derived cardiomyocytes (hiPSCM) reveal spontaneous rhythmic beating which can be monitored by impedance and microelectrode array recording of extracellular field potentials. Furthermore, the beat rate determines the duration of the field potentials (FPD) in a reverse use-dependent manner. However, to understand drug mediated frequency changes, hiPSCM require a frequency correction of the FPD/CTD according to experimentally determined restitution curves or, preferably, cells can be paced by electrical means to beat at a constant rate. To address this experimental limitation, we present a novel lipid-based transfection method which allows for a highly efficient and non-integrating optogenetic modification of Cor.4U® hiPSCM using channelrhodopsin-2 mRNA. First, channelrhodopsin-2 mRNA was transfected into hiPSCMs which were then cultured and measured on CardioExcyte NSP96 plates. The channelrhodopsin-2 enabled the cells to be paced by optical stimulation (blue light) at defined rates for more than 2 weeks using the new CE96 optical stimulation system currently under development for CardioExcyte. Importantly, cells followed pacing frequencies from 1.5 Hz up to 5 Hz (higher frequencies were not tested).

These data demonstrate novel tools to standardize, reduce costs, and greatly expedite drug safety screening in target organs of human origin while reducing animal usage. An important aspect of these studies is having proper quality control measures in place to guarantee consistent, reproducible results from lot to lot. At Axiogenesis, the CardioExcyte 96 is used literally every day to test our cells for adherence, physiology, beat rate regularity, and response to standard pharmacological benchmarks. These standards ensure the cells perform in your hands!

5. **Pharmacological Characterization of the NMDA A-B-C by Automated Patch Clamp**

Ilka Rinke, Søren Friis, Claudia Haarmann, Alison Obergrussberger, Michael George, Andrea Brüggemann, Niels Fertig

¹Nanion Technologies GmbH, Gabrielenstr. 9, 80636 Munich, Germany

N-Methyl-D-Aspartate receptors (NMDAR) are one of the key players in basic and complex excitatory neurotransmission. Seven subunits of NMDAR have been identified: GluN1,
GluN2A-D and GluN3A-B1. Assembled as a tetramer, they consist of two NR1 subunits and either two NR2 subunits or a combination of NR2 and NR3 subunits.

Unique properties of NMDAR are the activation of the channel by simultaneous binding of glutamate and glycine, a voltage-dependent block by magnesium ions, a relatively slow current kinetic and a predominantly calcium carried conductance. The exceptional calcium entry through open NMDARs triggers on the one hand a number of regulatory processes important in development and synaptic plasticity processes of learning and memory. On the other hand NMDARs are proposed to play a pathophysiological role in a number of neurological disorders such as epilepsy and Alzheimer’s. Given the importance in the treatment of such neurological diseases, it is of great interest developing clinically relevant NMDAR antagonists that would block excitotoxic NMDAR activation, without interfering with NMDAR function needed for normal synaptic transmission and plasticity.

This study focuses on the basic biophysical properties of different NMDAR subtypes and the pharmacological relevance of modulation of NMDARs. Among others, we show activation kinetics of GluN2A, GluN2B, GluN2C and GluN2D subunit containing NMDARs. Moreover, we present data from the target screen of the positive allosteric modulator CIQ and blockers which were recorded with high throughput. All experiments were performed on the SyncroPatch384PE, the only APC device, which is able to stack the solutions inside a pipette and rapidly apply it to the cell, allowing for brief and accurate solution exchange (<10ms) and exposure times (<200ms). NMDAR expressing cell lines were kindly provided by Chantest.

6. Activation of CFTR channels in absence of internal fluoride using a highly parallel automated patch clamp system

Andrea Brueggemann¹, Søren Friis¹, Tim Strassmaier², Markus Rapedius¹, Tom Goetze¹, Claudia Haarmann¹, Ilka Rinke¹, Atsushi Ohtsuki³, Takayuki Oka³, Marius Vogel¹, Timo Stengel¹, Johannes Stiehler¹, Michael George¹ and Niels Fertig¹

¹Nanion Technologies GmbH, Gabrielenstr. 9, 80636 Munich, Germany, ²Nanion Technologies USA, 1 Naylon Ave # 1, Livingston, NJ 07039, New Jersey, USA, ³Nanion Technologies Japan, MIL5, TWIns 3F, 2-2, Shinjyuku-ku, Tokyo, Japan

Cystic fibrosis is caused by malfunction of the chloride channel, Cystic Fibrosis Transmembrane Regulator (CFTR). CFTR is expressed in the apical membrane of epithelial cells where it is involved in the regulation of fluid transport across the epithelium. A large number of mutations of the protein are known to cause CFTR to become dysfunctional and only very few pharmaceutical compounds have been developed to treat the disease by restoring the chloride conductance of the channel. CFTR is activated by cAMP dependent phosphorylation and is gated by ATP. Activation is typically achieved using forskolin that activates adenylyl cyclase which leads to phosphorylation of the channel via protein kinase A (PKA). An alternative mode of activation is via application of intracellular F⁻.
However, intracellular F⁻ has also been widely used on most automated patch clamp (APC) platforms due to its stabilizing effects during the giga-seal formation. On the other hand, this also makes it difficult to control the degree of activation of the channel and represents a general limitation in the use of APC platforms in drug discovery for CFTR.

We now here present data from Nanion’s SyncroPatch 384PE where we activate the channel with forskolin under F⁻-free conditions at a high throughput. Further, CFTR could also be activated by first patching the cells in F⁻-free conditions and then exposing the cell to intracellular F⁻ using the internal solution exchange function. Our results show that the activation of CFTR by either forskolin or intracellular F⁻ is sensitive to Glibenclamide in a dose- and voltage-dependent manner. Taken together, these experiments firstly show a F⁻-free approach to study the pharmacology of CFTR at high throughput that might empower new methods CFTR drug discovery.

7. “The Importance of Being Earnest”: Ion Channel Assay Development Using the SyncroPatch

Andrew Allen, David Baez, and Jen Q Pan

Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA

Ion channels are essential for all life and are thus integral to human health. Recent efforts in human genetics have provided further insight into the role of ion channels in numerous diseases, posing them as high valuable drug targets. However, high throughput functional assessment of ion channels has remained elusive, as common cell-based assay platforms such as FLIPR are neither single-cell nor biophysically informative, and manual patch-clamp electrophysiology is not amenable to high throughput evaluation of hundreds of genetic variants or hundreds of thousands of compounds. Robotically-assisted high throughput single-cell planar patch-clamp electrophysiology platforms like the SyncroPatch offer a possible resolution to this problem, but immense challenges still remain in regards to cell line development, assay development, and data analysis, and these challenges are multiplied by the many different types of ion channels relevant to human health and disease, each presenting their own unique challenges. Here we present our comprehensive efforts thus far in assay development for the voltage-gated calcium channel Cav3.3, and our preliminary results in the development of assays for the voltage-gated sodium channel Nav1.2 and the glutamate-gated NMDA receptor. We will highlight the challenges both overcome and still remaining, and we hope to stimulate discussion of best practices for further development of the SyncroPatch as an essential tool for the routine throughput analysis of ion channels.
8. **High throughput real-time measurement of electrogenic membrane transport driven by the SLC transporters PepT1 and OcT2**

Maria Barthmes, Andre Bazzone, Stephan Holzhauser, Niels Fertig, Michael George1, Andrea Brüggemann

Nanion Technologies GmbH, Gabrielenstr. 9, 80636 Munich, Germany

“Solid Supported Membrane (SSM) based electrophysiology” is an established method, developed at the Max-Plank-Institut, which allows to record low amplitude electrogenic events with a high amplification. The method allows real-time activity measurement of targets for which conventional electrophysiology is unsuitable, like many electrogenic membrane transporters and pumps, or targets localized in intracellular or bacterial membranes. This is achieved by the use of a 1-3 mm gold electrode which is coated with an SSM and membrane vesicles or liposomes containing the target protein. The protein of interest is activated by a fast solution exchange. In eletrogenic transporters this generates a membrane potential, which can be measured at the electrode. The peak current is proportional to the turnover rate.


James Brady, Rama Shivakumar, Krista Steger, and Madhusudan Peshwa.

MaxCyte, Gaithersburg, MD, USA.

Cell-based assays using mammalian cells to express receptor targets are widely used to rapidly identify molecular mechanisms of human disease and to develop novel therapeutics. It is often challenging to engineer cells to co-express multiple transgenes and multiple protein complexes to generate these functional receptor assays. MaxCyte’s delivery platform for cell engineering enables the rapid and scalable expression of multi-subunit, complex membrane receptors in relevant cell types using Flow Electroporation™ Technology. In this poster, we demonstrate the high transfection efficiencies and cell viabilities for a variety of cell types, as well as illustrate the use of Flow Electroporation Technology for the development and screening of several ion channels and transporters.
Modeling heart disease with human iPSC-derived cardiomyocytes – first experiences with CardioExcyte96

Shan S. Parikh1,2, Lili Wang1,3, Kyungsoo Kim1,3, Kevin Bersell2, Tao Yang3, Marcia Blair3,2, Dan M. Roden3, Bjorn C. Knollmann1,3

1Vanderbilt Center for Arrhythmia Research and Therapeutics, Nashville, TN, 2Vanderbilt University School of Medicine, Nashville, TN, 3Department of Pharmacology and Medicine, Vanderbilt University Medical Center, Nashville, TN

Introduction: At VanCART, our mission is to investigate the underlying mechanisms of arrhythmias using both rodent and human cellular models. The development of academically generated human induced pluripotent stem cell (hiPSC) derived cardiomyocytes (CM) has revolutionized our ability to model disease. When coupled with recent gene editing techniques (such as CRISPR/Cas9), we are now able to generate isogenic controls from cells of patients with disease resulting in a powerful tool for cardiomyocyte specific mechanisms of disease pathogenesis. Current gold standard techniques for the investigation of cellular contractility and electrophysiological activity has relied primarily on single cell assessment using edge detection via the IonOptix system and patch clamp respectively. However, these techniques are technical challenging and rather tedious. To assess the pathogenicity of the increasing number of novel mutations it is imperative that we adopt better methods to screen disease outcomes in a reliable fashion before moving to single cell analyses.

Purpose: To assess the relationship between gold standard techniques for measuring single cell contractility and electrophysiological based parameters to high-throughput methods which generate impedance and extracellular field potential (EFP) measurements.

Methods: Day 30 hiPSC-CM generated using standard chemical differentiation methods were utilized for the following techniques. For single cell assessment of contractility, d30 cells were plated on flexible Matrigel substrate and allowed to mature for 5 days prior to edge detection assessment of Fura2 loaded cells using the IonOptix instrument. Electrophysiological measurements of action potential were completed using patch clamp. Semi-simultaneous measurement of impedance and EFP was performed on the CardioExcyte96 (Nanion).

Results: For comparison of contractility based parameters to impedance, two models of cardiomyopathy were utilized (HCM and DCM). Results of impedance based measurements were found to be comparable to that of single cell measurements in both lines. A mutation causing variability in action potential (AP) duration was utilized for comparison of EFP data to patch clamp data, which also demonstrated similarities between variability of AP duration and field potential duration. In conclusion, we have begun to employ the CardioExcyte96 for assessment of contractility and electrophysiological based parameters and find it provides comparable results for parameters of interests and will be a valuable tool for future screening of disease causing mutations.
11. Automated Patch Clamp studies of Ca$^{2+}$- activated Cl$^-$ channel TMEM16A (ANO1) using the SyncroPatch 384PE

Andrea Brueggemann$^1$, Tom Goetze$^1$, Markus Rapedius$^1$, Ilka Rinke$^1$, Claudia Haarmann$^1$, Timo Stengel$^1$, Johannes Stiehler$^1$, Marius Vogel$^1$, Torsten Ertongur-Fauth$^2$, Michael George$^1$ and Niels Fertig$^1$

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Ca$^{2+}$-activated chloride channels (CACCs) are expressed in various tissues and fulfill important, physiological functions from epithelial fluid transport to sensory transduction and modulation of action potentials in hippocampal neurons. Two members of a transmembrane protein family – TMEM16A and B – have recently been identified and characterized as essential subunits of CACCs [1]. Due to their anion/Cl$^-$ permeability and 8 trans-membrane domain structure they are also known as Anoctamin 1 and 2. They are activated by sub-micromolar concentrations of intracellular free Ca$^{2+}$ and can be blocked by classical Cl$^-$ channel blockers like niflumic acid. Over expression of TMEM16A was reported in esophageal squamous cell carcinoma and breast cancer progression. And not only for this reason it is an important target for the pharmaceutical industry.

Here was present electrophysiological data of TMEM16A using the SyncroPatch384PE, our device for high-throughput, automated patch-clamp measurements with 384 truly parallel amplifiers and versatile options for a fast and reliable internal perfusion.

12. MYH7-R403Q Patient-Derived iPSC Cardiomyocytes as a Model of Hypertrophic Cardiomyopathy

Hannah Fandl, Ted Kaplan, Michael Dunn, Lori Morton, Scott MacDonnell

Cardiovascular Research TFA, Regeneron Pharmaceuticals, Inc., Tarrytown, NY

Hypertrophic cardiomyopathy (HCM) affects 1 in 500 people worldwide, with no discrimination for race or gender. HCM is caused by the enlargement of cardiomyocytes, resulting in thickening of ventricular walls. This thickening reduces left ventricle chamber size and impairs relaxation, eventually resulting in reduced cardiac output, fibrosis, arrhythmia, and failure. The most prevalent form of the disease results from a missense mutation in the MYH7 gene (R403Q). Due to the limited availability of isolated adult cardiomyocytes to explore the poorly characterized functional and molecular mechanisms responsible for HCM, human induced pluripotent stem cell-derived (hiPSC-derived) cardiomyocytes have been developed. While hiPSC-derived cardiomyocytes are being utilized as a source of human cardiomyocytes, their utility for exploring diseased phenotypes remains incompletely characterized. Therefore, the purpose of the current study was to profile hiPSC-derived cardiomyocytes from a healthy patient and a HCM patient with the R403Q mutation using a novel impedance based platform. Methods: hiPSC-derived cardiomyocytes from both
Healthy and MYH7-R403Q patients were purchased from Cellular Dynamics International. Cells were seeded and profiled using the Nanion CardioExcyte96. Impedance measurements to assess contractile function and extracellular field potential (EFP) to evaluate action potential duration were collected. Results: Reduced impedance amplitude and lower intrinsic beat rate were observed in MYH7-R403Q vs. healthy hiPSC-derived cardiomyocytes. No difference in beat rate regularity (index of arrhythmia) was observed. Reduced contraction rise time and increased fall time were observed for the MYH7-R403Q vs. healthy. MYH7-R403Q cells demonstrated increased EFP duration vs. healthy.

Conclusions: A platform to functionally characterize contractility and EFP of hiPSC-derived cardiomyocytes has been developed. Distinct differences were observed between healthy and MYH7-R403Q hiPSC-derived cardiomyocytes. The establishment of a platform to phenotypically define diseased cardiomyocytes provides a relevant in vitro model to explore the biological mechanism(s) behind human genetic cardiomyopathies and may allow for the identification and advancement of novel therapies.
Event Area Map
Thank you for attending our User Meeting!

- Your Nanion Team