ELECTROPHYSIOLOGY IN IPSC DERIVED NEURONS AND CARDIOMYOCYTES: MICROELECTRODE ARRAY (MEA), OPTOGENETICS AND AUTOMATED PATCH-CLAMP APPROACHES

Elena Dragicevic[1], Krisztina Juhasz[1], Ulrich Thomas[1], Isaac Clements[2], Daniel Millard[2], Anthony Nicolini[2], Stacie Chvatal[2], Sonja Stölzle-Feix[1], Nadine Becker[1], Leo Doerr[1], Markus Rapedius[1], Claudia Haarmann[1], Tom Goetze[1], Matthias Beckler[1], Michael George[1], Andrea Brüggemann[1], Niels Fertig[1]

[1]Nanion Technologies, Munich, Germany;

[2]Axion BioSystems, Inc., Atlanta, GA, USA

Reliable and fast in-vitro drug safety and discovery screening demand development of automated, high-throughput compatible evaluation systems. Resent rise in usage of iPSC derived cardiomyocytes and neurons provided more predictive models for assessment of invitro assays. Together, automated, high-throughput electrophysiological assays and iPSCs offer easy to use format for both academic research as well as pharmaceutical industry to perform screening of new drug candidates in a physiologically relevant environment.

We show complementary electrophysiology platforms, which provide unmatched information on a compound's safety profile. Reduced cell usage, increased throughput and integration into robotic environments improve cost efficiency, precision and are speeding up the HTS process of drug development and safety screening. We describe the development and optimization of cell-based assays that are sensitive and provide reproducible results for safety pharmacology. We present evaluation data from four major systems performed on iPSCs, giving information on ionic currents, action potentials and activity patterns. Changes in the impedance signal indicate effects on cell contractility and shape whereas the field potential parameters provide information about the electrophysiological activity of the beating network of cells.

In accordance with the Comprehensive In Vitro Proarrhythmia Assay (CiPA) guidelines, standard reference compounds were tested on iPSCMs. Example traces of action potential recordings, voltage-clamp measurements and also contractility and EFP/MEA recordings before and after compound applications were compared. Additionally, we show a successfully optically-integrated multiwell MEA system with selective control over cultured network activity, which enables advance in vitro modelling and modulation of electrical phenotypes for diseases such as epilepsy, autism, Alzheimer's and ALS as well as cardiac arrhythmias. Our findings demonstrate the potential of optically-integrated multiwell MEA systems to enable high-throughput drug screening and phenotypic modelling of diseases.