BRIDGING HTS ION CHANNEL AND MYOCYTE DATA

George O. Okeyo[1], Sonja Stoelzle-Feix[2], Timothy Strassmaier[1], Krisztina Juhasz[2], Nadine Becker[2], Ulrich Thomas[2], Leo Doerr[2], Markus Rapedius[2], Nina Brinkwirth[2], Claudia Haarmann[2], Tom Goetze[2], Matthias Beckler[2], Michael George[2], Andrea Brüggemann[2], Niels Fertig[2]

[1]Nanion Technologies Inc., Livingston, NJ, USA,
[2]Nanion Technologies GmbH, Ganghoferstrasse 70A, 80339 Munich, Germany.

Human induced pluripotent stem cells (hiPSCs) are relevant for cardiac safety testing due to their validated predictivity as described in recent publications derived from the comprehensive in vitro proarrhythmia assay (CiPA) study. We combined automated patch clamp (APC), impedance and extracellular field potential (EFP) measurements to study cardiac ion channels in cell lines and hiPSC-CMs.

Cell lines expressing different cardiac ion channels were recorded on two different APC instruments (8 or 384 wells simultaneously) at room and physiological temperature, at 4 different sites. Within the myocyte validation study of the CiPA initiative, hiPSC-CMs from different providers were used on a device combining impedance-based contractility and extracellular field potential (EFP) recordings. Within the ion channels working group of the CiPA initiative, ion channel data on 7 cardiac ion channel currents were measured. The effects of >20 CiPA reference compounds deemed low, intermediate and high risk by the FDA were investigated. In parallel to APC investigations, arrhythmogenicity of this and other compounds were investigated via contractility and field potential recordings in 2D monolayers of iPSC-CM.

Our results show that high risk compounds such as dofetilide prolong field potential duration which resulted in the detection of arrhythmic events in both impedance and EFP recordings. Datasets from multiple sites and cell types will be shown and compared. Cross-site/cell comparisons of APC ion channel data and myocyte repolarization data was combined in order to investigate the mode of action of reference compounds. This promotes a good understanding of drug-induced arrhythmia and thus represents a valuable approach in drug development efforts.