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Impedance and Extracellular Field Potential for Cardiac Safety Assays: A Combined Approach for Non-Invasive Screening of iPS Cells

Corina T. Bot[2], Sonja Stölzle-Feix[1], Nadine Becker[1], Ulrich Thomas[1], Krisztina Juhasz[1], Leo Doerr[1], Matthias Beckler[1], Michael George[1], Andrea Brüggemann[1], Rodolfo Haedo[2], Niels Fertig[1]

[1]Nanion Technologies, Gabrielenstr. 9, 80636 Munich, Germany

[2]Nanion Technologies Inc., 1 Naylon Place, Livingston, NJ, 07039, USA

A drug candidate's capacity to interact with ion channels involved in the depolarization or repolarization phases of the cardiac action potential is important for drug safety assessment. More specifically, drug-induced arrhythmia is one of the most common causes of drug development failure.

In recent years, human stem cell-derived cardiomyocytes have proven to recapitulate key features of human cardiac electrophysiology in vitro. In accordance with the Comprehensive In Vitro Proarrhythmia Assay (CiPA) guidelines, we present data recorded on Nanion's CardioExcyte 96. A non-invasive deconvolution of a compound mechanism of action with the CardioExcyte96 is presented.

The CardioExcyte 96 is a hybrid screening instrument that combines impedance with MEA-like extracellular field potential (EFP) recordings. Changes in the impedance signal indicate effects on cell contractility and overall shape, whereas the field potential parameters provide information about the electrophysiological activity of the beating network of cells. Furthermore, it has become apparent that the intact ensemble of cardiac ion channels is necessary to determine proarrhythmic effects reliably.

We present pharmacological investigations of reference compounds (e.g. Dofetilide, Nifedipine, Verapamil) on cardiac contractility and EFPs of iPS cardiomyocytes. Cytotoxic responses of cell monolayers involve metabolic or biochemical changes that affect the morphology of the cells, or reduce their overall viability. Pharmacological effects of a number of reference compounds tested for long-term cytotoxicity in non-excitable cells will also be presented.

This approach strengthens the importance of testing compounds in assays complementary to patch clamp electrophysiology, to provide a more complete safety profile.