Combined impedance and extracellular field potential recordings on iPS cardiomyocytes

Krisztina Juhasz¹,², Sonja Stölzle-Feix¹, Corina Bot³, Nadine Becker¹, Ulrich Thomas¹, Leo Doerr¹, Elena Dragicevic¹, Matthias Beckler¹, Michael George¹, Andrea Brüggemann¹, Niels Fertig¹

¹ Nanion Technologies, Munich, Germany
² Technical University of Munich, Munich (Germany)
³ Nanion Technologies Inc., Livingston, NJ, 07039 (USA)

Motivation:

Drug induced arrhythmia is one of the most common causes of drug development failure. Human induced pluripotent stem cell-derived cardiomyocytes (iPSCMs) have a great potential for cardiovascular research and predictive in-vitro cardiac safety screening when it comes to early detection of arrhythmic compounds.

Material and Methods:

The CardioExcyte 96 system provides a non-invasive, label-free, high temporal resolution approach for safety screening on iPSCMs. It is a hybrid screening instrument that combines impedance with MEA-like extracellular field potential (EFP) recordings. Furthermore, it can be either used in an incubator or, by utilizing the dedicated incubation system, directly on a lab bench. The system is capable of electrically pacing the cells, which allows for screening of cells which beat with individual frequencies and, in addition, investigations of frequency dependent compound inhibition.

Results:

We describe the development and optimization of a cell-based assay that is sensitive and provides reproducible results for safety pharmacology. 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 iPS-derived cardiomyocytes.
Table 1: Changes of human-induced pluripotent stem cell-derived cardiomyocytes (Cor.4U) beating pattern measured by impedance and extracellular field potential methods.

Discussion:

We have shown combined impedance and EFP measurements using a commercially available platform (CardioExcyte 96) can be made reliably from a number of different hiPSC-CMs including Cor.4U (Axiogenesis AG), iCell Cardiomyocytes (Cellular Dynamics International), Pluricytes (Pluriomics) and Cellartis® hiPS-CM (Takara Bio Europe AB). These cells are becoming increasingly important for cardiac safety testing due to their abundance, purity, recapitulation of native behavior and suitability for HTS techniques.

Conclusion:

The CardioExcyte 96 is, so far, the only platform on the market capable of recording in combination impedance and EFP measurements from same cell. This provides a unique opportunity to detect changes in both contractility and ion channel function at a high throughput which may prove crucial for cardiac safety screening particularly in the light of the new CiPA guidelines.

Acknowledgements:

We thank Cellular Dynamics International, Madison, WI, for the collaboration and for providing us with cardiomyocytes (iCell cardiomyocytes) and Axiogenesis AG, Cologne, Germany, for the collaboration and for providing us with cardiomyocytes (Cor.4U). We thank Pluriomics for providing us with the Pluricytes and Takara Bio Europe AB for providing Cellartis® hiPS-CM.