

“All Inclusive approach” for electrophysiological high-throughput screening and drug discovery using iPS derived cardiomyocytes

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Drug discovery major challenges focus mainly on predictability of proarrhythmic effects in safety screening. The Comprehensive in Vitro Proarrhythmia Assay (CiPA), an FDA-directed initiative, is specifically focused on improved preclinical assessment of torsade de pointes (TdP) risk, striving to optimize the drug discovery process. In recent years, human induced pluripotent stem cell-derived cardiomyocytes (iPSCMs) have proven to recapitulate key features of human cardiac electrophysiology *in vitro*. Furthermore, it has become apparent that the intact ensemble of cardiac ion channels is necessary to determine proarrhythmic effects reliably. Hence, due to their increasing availability, stem cell-derived cardiomyocytes have become the preferred choice of cardiac cells. For this purpose we have developed cell handling protocols for the use of iPSCMs on planar patch clamp systems of medium and high throughput, including pharmacological data on voltage-dependent channels of the CiPA panel at different temperatures. Additional data was generated on a hybrid screening instrument that combines impedance (cell contractility) with MEA-like extracellular field potential (EFP) providing a non-invasive, label-free, high temporal resolution approach for drug and safety screening on iPSCMs. Furthermore, we demonstrate novel solutions for specific cell stimulation (pacing) using multiwell light delivery add-ons for optogenetics.