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Disease modelling, safety screening and drug development using IPSCs: Automated patch clamp, extracellular field potential and impedance platforms

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Electrophysiological characteristics and activity footprint of induced pluripotent stem cell (iPSC) derived cardiomyocytes and neurons, recently became a priority in disease modeling research, 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 automated patch-clamp and MEA systems performed on iPSC cardiomyocytes, 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 demonstrate the application for the MEA systems for usage of iPSC derived neurons in drug development and characterization of in vitro disease models – Parkinson´s disease, ALS, epilepsy, fragile X, and autism – with the ultimate goal of identifying treatments. The high throughput, ultra-high resolution (millisecond events with microvolt amplitudes), high electrode count (allows population network activity measurements) and accuracy these systems provide will significantly accelerate progress toward such treatments. Multiwell optogenetic stimulation further excels MEA-based disease modeling and drug discovery.

In summary, we show complementary electrophysiology platforms, which provide unmatched information on a compound's safety profile, drug discovery and development of phenotypic disease-in-a-dish cellular models. Reduced cell usage, increased throughput and integration into robotic environments improve cost efficiency, precision and are speeding up the whole HTS process of drug development and safety screening