ADVANCING DRUG DISCOVERY AND DISEASE MODELING: AUTOMATION AND OPTOGENETICS FOR PATCH-CLAMP AND MEA TECHNOLOGY

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In the constantly evolving field of drug discovery and safety, novel technologies and application have become a priority. Here, we describe diverse approaches and present data dissecting electrophysiological characteristics and activity patterns of different iPSCs. We present novel additions, enabling researchers to elevate their assays to a higher level, using automation and optogenetics as powerful tools to increase throughput and obtain more freedom in experimental design.

The need for simple, reliable and predictive pre-clinical assays for cardiac safety has motivated initiatives worldwide including the Comprehensive in vitro Proarrhythmia Assay (CiPA). Automated high throughput planar patch clamp systems complement this need. Specialized protocols for reduced cell usage, increased throughput and integration into robotic environments improve cost efficiency, precision and are speeding up the HTS process of drug development and safety screening. Additionally, pioneering the fully automated MEA system, integrating MEA plate preparation, maintenance and full MEA assay execution, complement automated patch-clamp measurements. This system seamlessly integrates a sterile compact workstation, which includes a robotic liquid handler, 44-plate capacity incubator, environmental controller and HEPA filtration system. Here, we present the data obtained during Phase II of the CiPA initiative study, performed using these two automation systems and diverse iPSC derived cardiomyocytes. Both approaches demonstrated high throughput, sensitive and reproducible performance on various sites.

Furthermore, we demonstrate novel solutions for specific cell stimulation (pacing) or silencing using multiwell light delivery add-ons for optogenetics. Multiwell optogenetic stimulation further excels impedance and MEA-based disease modeling and drug discovery. Through even illumination of the wells and lack of induced artifact, optogenetic stimulation exhibits improved reliability across wells, as compared to electrical stimulation.
In summary, we present novel experimental possibilities by incorporating automation and optogenetics approaches into already available and widely used technologies, yielding higher throughput, sensitivity and precision.