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ADVANCES IN AUTOMATION AND OPTOGENETIC STIMULATION FOR PATCH-CLAMP AND MEA TECHNOLOGIES FOR DRUG DISCOVERY AND DISEASE MODELING

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Advancements in drug discovery and safety dictate constant development of hardware necessary to yield high throughput, sensitivity and precision of pre-clinical assays on iPSC-derived cardiomyocytes and neurons. Here, we show complementary electrophysiological pre-clinical assays, which are simple, reliable and highly predictive. We focus primarily on cardiac safety applications, as introduced through Comprehensive in vitro Proarrhythmia Assay (CiPA) worldwide initiative. For this purpose, we have developed specialized protocols and show data from diverse iPSC derived cardiomyocytes on automated high throughput planar patch clamp systems, in order to reduce cell usage and increase throughput. Integration into robotic environments improved cost efficiency, precision and speeded up the HTS process of drug development and safety screening. Complementary to HTS automated patch clamp assays, we show the CiPA Phase II study results, obtained on a fully automated MEA system, integrating MEA plate preparation, maintenance and full MEA assay execution. This system integrates a sterile compact workstation, with a robotic liquid handler, 44-plate capacity incubator, environmental controller and HEPA filtration system. Both approaches demonstrated high throughput, sensitive and reproducible performance at 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 artifacts, optogenetic stimulation exhibits improved reliability across wells, as compared to electrical stimulation. In summary, 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.