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ELECTROPHYSIOLOGY IN IPSC DISEASE MODELING: MICROELECTRODE ARRAY (MEA) OPTOGENETICS AND AUTOMATED PATCH-CLAMP APPROACHES

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Dissecting electrophysiological characteristics and distinct activity patterns of induced pluripotent stem cell (iPSC) derived neurons, recently became a priority in disease modeling research. Here, we describe different electrophysiological methods, used to achieve this goal. Multi-well microelectrode array (MEA) systems (Axion Biosystems) provide simultaneous measurements of extracellular electrophysiological activity of excitable cells over long periods of time. Each electrode is capable of capturing extracellular action potentials of excitable cells in ultra-high resolution (millisecond events with microvolt amplitudes), while multiple recording sites within each well allow population network activity measurements. MEAs offer unbiased, label free, non-invasive recordings of natural cell functions, in a regulated physiological environment. Multiwell optogenetic stimulation further excels MEA-based disease modeling and drug discovery. These features enabled the usage of MEAs in 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 and accuracy that Axion's MEA systems provide will significantly accelerate progress toward such treatments. Automated, high-throughput planar patch clamp systems (Nanion Technologies), complement the need for predictive neurotoxicity screening in-vitro assays. 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 as a whole. Our special cell handling protocols enable usage of both control and patient derived, iPSC derived neurons on planar automated patch clamp systems. Our chip-based approaches, allow parallel patch clamp recordings without compromising neither data quality nor sophistication regarding technical features.
In summary, we present the data obtained from neuronal disease modelling experiments, by using both MEA and automated patch clamp approaches. These platforms together provide unmatched possibilities to study specific neurological disorders by developing phenotypic disease-in-a-dish cellular models.