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FUNCTIONAL CHARACTERIZATION OF HUMAN IPSC-DERIVED NEURONAL NETWORKS USING HIGH-DENSITY MICROELECTRODE ARRAYS

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The advent of iPSC technology paved the way to studying and characterizing human cells *in vitro*. The technology enabled the generation of human neurons, which can be functionally characterized by microelectrode array technology. High-density microelectrode array (HD-MEA) technology allows for investigating neuronal electrophysiology at high spatial and temporal resolution. The main goal of this work was to combine HD-MEA and iPSC technologies, in order to assess and compare electrophysiological properties and functional phenotypes of human iPSC-derived neuronal lines (motor neurons and dopaminergic neurons) and related disease-model lines (Parkinson's disease and amyotrophic lateral sclerosis). Using a CMOS-based 26'400-electrode HD-MEA, we investigated standard metrics (e.g., spike rate) and network electrophysiology metrics (e.g., burst rate) by recording from hundreds of neurons simultaneously. The aim was to distinguish functional network phenotypes of the corresponding human iPSC-derived neuronal cell lines.
Comparing the isogenic dopaminergic neuron lines, we observed that control iCell® DopaNeurons and the disease line A53T MyCell® DopaNeurons could be discriminated by standard HD-MEA metrics. Specifically, the two dopaminergic neuronal lines showed different spike rates, spike amplitudes and inter-spike intervals. Furthermore, the two dopaminergic neuronal lines largely differed in burst durations and inter-burst intervals. Similar results were found with the motor neuron isogenic lines iCell® Motor Neurons and MyCell® Motor Neurons, which could be differentiated by their spike rates and inter-spike intervals. The healthy cells had a higher spike rate than the disease line at DIV 14. The two motor neuronal cell lines showed also significantly different burst durations and inter-burst intervals. Lastly, we analyzed the network burst shapes and found that this metric could be used to differentiate all healthy and disease lines at any day in vitro.
In this work we demonstrated that by analyzing MEA metrics, it was possible to characterize and distinguish healthy and diseased dopaminergic and motor neuronal cell lines. In particular, metrics, such as spike rate and burst duration, hold great potential to assess cell excitability or network synchronicity in case of disease.

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