

### ➤ Neurotoxicology screening using a high-sensitivity MEA platform

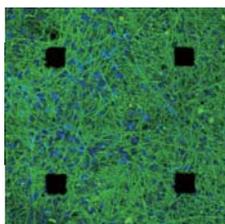
**Functional networks** of human induced pluripotent stem cell-derived (hiPSC) neurons are potentially powerful in vitro models for drug and neurotoxicity screening. Determining the potential for a compound to cause (or prevent) adverse neurophysiological events is enormously valuable. However, a high-sensitivity physiological assay is necessary for detecting subtle events that underlie pathophysiological states. In this study, we cultured hiPSC neurons and recorded their activity using the MED64 Presto high-throughput microelectrode array (MEA) system. hiPSC neurons were plated in 24-well MEA plates in order to simultaneously record extracellular potentials before, during and after drug application. After application of anti-convulsant drugs, we show that the MED64 Presto system, in combination with cultured human iPSC neurons, is highly sensitive to changes in neural activity and is able to successfully identify potential therapeutic drugs.



MED64 Presto



MEA 24well Plate



iPSC-neurons cultured on a MEA

#### ➤ Toxicity screening using iPSC neurons

Epileptiform activity is one marker of neuronal toxicity. We examined chemically evoked epileptiform activity, induced by 4-Aminopyridine (4-AP), pilocarpine, chlorpromazine, and pentylentetrazole (PTZ). After application of convulsant drugs, the high-sensitivity of the MED64 Presto allowed for the observation of hallmarks of epileptiform activity -- increased duration and number of bursting and synchronized bursting activities. Additionally, using known anti-convulsants, we observed a reversal of epileptiform activity in a dose-dependent manner.

#### ➤ Material & Methods

##### Human iPSC-derived neurons and astrocytes

Human iPSC-derived cortical neurons (Axol Bioscience) were cultured at density of  $8.0 \times 10^5$  cells/cm<sup>2</sup> on the MEA electrodes. After 8 days in culture, Human iPSC-derived mature astrocyte (Axol Bioscience) were added at a concentration of  $1.0 \times 10^5$  cells/well.

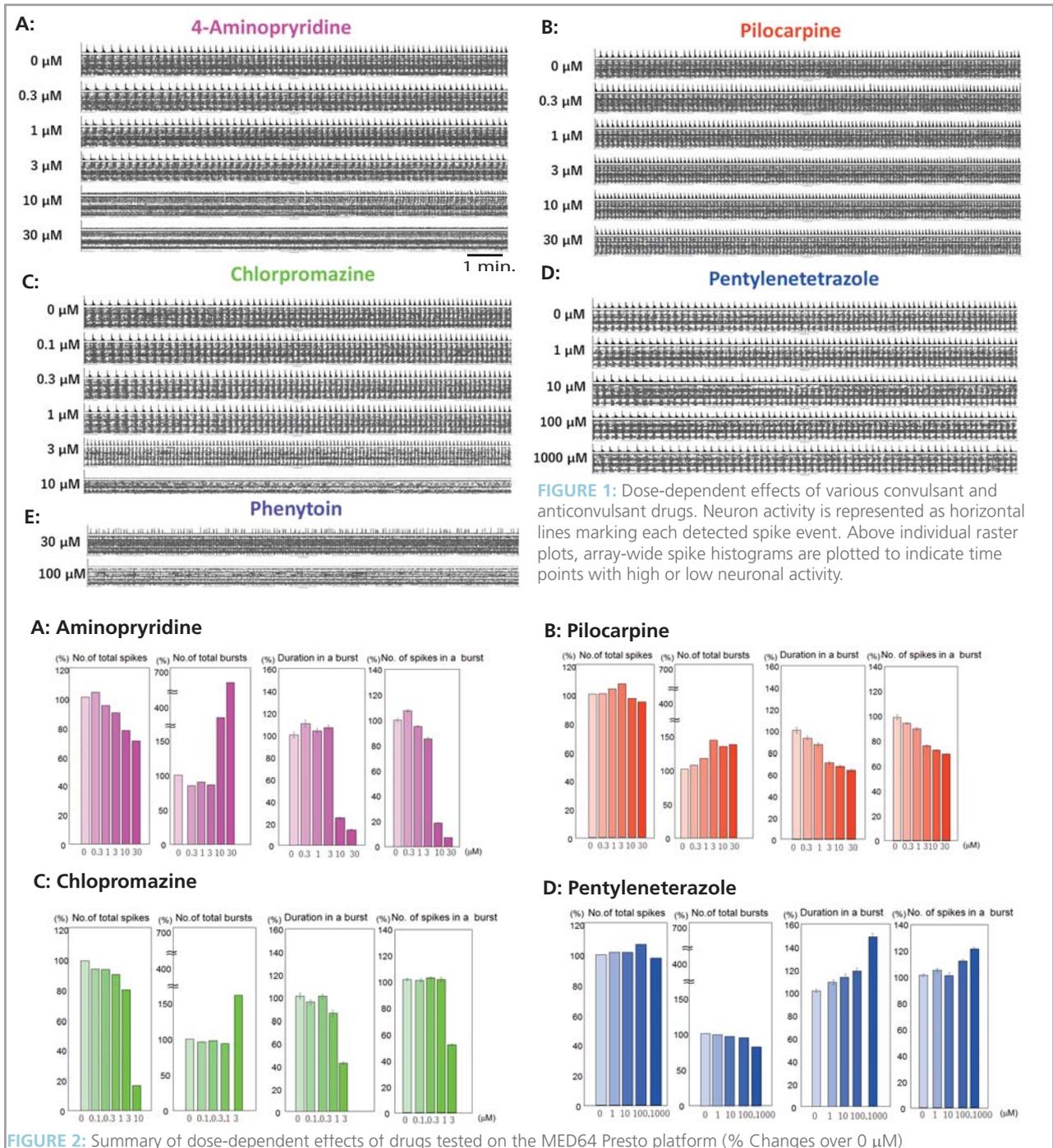
To investigate pharmacological effects, we administered 4-aminopyridine (0, 0.3, 1, 3, 10, 30  $\mu$ M), pilocarpine (0, 0.3, 1, 3, 10, 30  $\mu$ M), chlorpromazine (0, 0.1, 0.3, 1, 3, 10  $\mu$ M), pentylentetrazole (0, 1, 10, 100, 1000  $\mu$ M), and phenytoin (0, 1, 3, 10, 30, 100  $\mu$ M). Spontaneous firings were recorded for 10 min at each concentration and repeated during weeks 12-19 in culture.

##### Electrophysiology recording using High throughput MEA Platform

To evaluate the electrophysiological responses to drugs, we used a high throughput planar MEA measurement system (Presto, Alpha MED Scientific, Japan). The MEA plates contain 384 electrodes in a 24-well format. Each well contains 16 low-impedance electrodes that exhibit a high signal-to-noise ratio. Spike analyses were performed using MED Symphony and Mobius Offline Toolkit softwares (Alpha MED Scientific).



## ► Induction of Epileptiform Activities and Effects of Anti-convulsant Drug in Human iPSC-neurons



Data: provided by Ikruo Suzuki, PhD, Tohoku Institute of Technology

## ► MED64 Presto: High-Sensitivity Microelectrode Array Platform

MED64 systems are the most sensitive MEAs on the market. The combination of its high sensitivity and broad acquisition bandwidth results in lower noise for more accurate recordings. The plate-style format of the MED64 Presto increases the number of electrophysiology experiments that can be performed in a day and promotes productivity.

Further information: [www.med64.com](http://www.med64.com)



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