News Release

Ricoh Co., Ltd.

Elixirgen Scientific, Inc.

Offering assay-ready multi-electrode array plates to measure electrical activities of human iPS cell-derived neurons

- Simplify drug efficacy and neurotoxicity evaluation -

TOKYO, Japan - *December 3, 2020* - Ricoh Co., Ltd. (Tokyo, Japan) and Elixirgen Scientific, Inc. (Baltimore, Maryland, USA) have jointly developed assay-ready cell plates, which may dramatically simplify the drug efficacy testing for neurological diseases and the neurotoxicity testing for chemical compounds. This product contains human neurons generated from human induced pluripotent stem (iPS) cells using Elixirgen Scientific's cell differentiation technology. These human neurons are firmly attached to the surface of multi-electrode array plates using Ricoh's bioprinting technology. The plates are ready to use for a variety of biomedical applications, including the measurement of electrophysiological activities of human neurons exposed to various drugs and compounds. We begin supplying samples of assay-ready multi-electrode array plates to pharmaceutical companies and research institutions, aiming to start product sales and service contracts to evaluate drug efficacy and toxicity for human neural tissues before April 2021.

One of the challenges for pharmaceutical industries is a high attrition rate of drug candidates due to its neurotoxicity uncovered only at the late preclinical stage or at the clinical trial stage. Toxicity evaluations are generally conducted using animal subjects. However, as humans differ from other animal species, animal models may not be able to predict the toxicity accurately. In particular, candidate drugs for neurological diseases often see their development discontinued during clinical studies because of toxicity. Therefore, a cell plate on which human neurons are grown, begins to be used for evaluating drug's effects and toxicity. Increasing the reliability of testing neurotoxicity using human neurons cultured in vitro can potentially reduce the cost and time for drug development. Therefore, development is vigorously underway for neural toxicity evaluation systems that use nerve cells derived from human iPS cells. For example, drug's efficacy and toxicity are evaluated using plastic plates with human nerve cells seeded on the electrodes, which allows the measurement of electrical activities of neurons exposed to the drug.

A human drug efficacy and toxicity evaluation plate is created by seeding test object nerve cells over a plate called a Multi-Electrode Array (MEA) with minute electrodes indwelled on the bottom of each well. It can measure and record nerve cell activity as electric signals. Production of nerve cell plate by the users themselves involves tremendous labor, cost, and risks, including cell culture know-how, a prolonged culture period, and problems such as agglutination and stripping off cells. Nerve cell plates are being sought that

require no cultivation and can be used quickly. Unfortunately, however, they have not been realized until now because of problems with quality instability and cells stripping off of the electrodes during transport.

Ricoh and Elixirgen Scientific have developed a transportable human neural drug efficacy and toxicity evaluation plate with dramatically enhanced cell adhesive properties. To produce nerve cells, we employed Elixirgen Scientific's technology, which can differentiate iPS cells into intended cells in a short period with a high level of efficiency. We also applied the cell adhesion coating technology that Ricoh cultivated through its bioprinting operations to investigate cells' adhesion to the electrodes and the cultivation conditions. Stabile product quality was achieved by optimizing various conditions. The results of post-transport tests simulating domestic transport also showed normal cell properties, making it possible to transport the human neural drug efficacy and toxicity evaluation plates to customers in a ready-to-use state. These achievements are expected to contribute dramatically to reducing the cost and risks of new drug development.

Moving forward, we will continue to develop plates that cater to customer needs, not only by incorporating the same cells but also by reproducing nerve networks using bioprinting technology.

* This product is a research reagent.

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Ricoh Announces Strategic Business Partnership with Elixirgen Scientific

https://www.ricoh.com/release/2019/0619_1/

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