High-Throughput Fluorescence Measurements of Action Potential and Ca²⁺ Transients in Human iPSC-Derived Cells for Toxicity Screening and Drug Discovery

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1. High-throughput fluorescence measurements of action potential and Ca²⁺ transients in human iPSC-cardiomyocytes

Human iPSC-derived cardiomyocyte (hiPSC-CM) is considered a novel promising tool for preclinical assessment of drug-induced cardiotoxicity, and various methods and platforms have been examined to evaluate cardiotoxic risks of drug candidates using hiPSC-CM. Among them, the use of fluorescent dyes to measure membrane action potential and Ca²⁺ transient is considered most suitable for high-throughput measurements, for example, in the case of toxicity screening.

We established experimental protocols to measure membrane potential changes and Ca²⁺ transients in hiPSC-CM (iCell® Cardiomyocytes², CDI) with a voltage-sensitive fluorescent dye (FluoVolt) and a calcium-sensitive fluorescent dye (Cal-520), respectively, on a kinetic plate reader, Hamamatsu FDSS/μCELL.

2. Detection of drug-induced beat rate changes, early-after depolarization (EAD)-like waveforms and so on in hiPSC-cardiomyocytes

Effects of various cardiotoxic compounds on membrane potential- and Ca²⁺ transient waveforms were measured. Results of 36 compounds are summarized in Table 1.

3. Detection of drug-induced synchronization of Ca²⁺ oscillation in human iPSC-derived mixed cortex neurons

Human iPSC-derived cortex neurons were cultured on 384-well plates according to the manufacturer’s instruction. On the day 43 after seeding, the cells were labeled with 2 μM Cal-520 (AAT Bioquest) for 45 min. Then, the compounds were added and incubated for 20 min. Ca²⁺ transients in human iPSC-derived neurons with FDSS/μCELL.

Summary

1. Membrane potential changes and Ca²⁺ transients in human iPSC-derived cardiomyocytes were measured with fluorescent dyes in the high-throughput manner using a kinetic plate reader, Hamamatsu FDSS/μCELL. Drug-induced various waveform changes were obtained.

2. We detected the drug-induced synchronization of Ca²⁺ oscillations in human iPSC-derived neurons with FDSS/μCELL.

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