An Automated Platform for Assessment of Congenital and Drug-Induced Arrhythmia with hiPSC-Derived Cardiomyocytes.

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Funding Grants: Improving Existing Drugs for Long QT Syndrome type 3 (LQT3) by hiPSC Disease-in-Dish Model

Public Summary:
The ability to produce unlimited numbers of human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CMs) harboring disease and patient-specific gene variants creates a new paradigm for modeling congenital heart diseases (CHDs) and predicting proarrhythmic liabilities of drug candidates. However, a major roadblock to implementing hiPSC-CM technology in drug discovery is that conventional methods for monitoring action potential (AP) kinetics and arrhythmia phenotypes in vitro have been too costly or technically challenging to execute in high throughput. Herein, we describe the first large-scale, fully automated and statistically robust analysis of AP kinetics and drug-induced proarrhythmia in hiPSC-CMs. The platform combines the optical recording of a small molecule fluorescent voltage sensing probe (VoltageFluor2.1.Cl), an automated high throughput microscope and automated image analysis to rapidly generate physiological measurements of cardiomyocytes (CMs). The technique can be readily adapted on any high content imager to study hiPSC-CM physiology and predict the proarrhythmic effects of drug candidates.

Scientific Abstract:
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