Publication

Electrophysiological characteristics and pharmacological sensitivity of two lines of human induced pluripotent stem cell derived cardiomyocytes coming from two different suppliers.

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J Pharmacol Toxicol Methods. 90:58-66 2018.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Electrophysiological+characteristics+and+pharmacological+sensitivity+of+two+lines+of+human+induced+pluripotent+stem+cell+derived+cardiomyocytes+coming+from+two+different+suppliers.

Abstract

Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) are increasingly used as preclinical tool for predicting drug-induced QT prolongation and arrhythmias. This study was conducted to assess the electrophysiological characteristics and the pharmacological sensitivity of two commercialized hiPSC-CMs. The baseline electrophysiological characteristics measured with a multi-electrode array (MEA) technology differ between Cor.4U and iCell2: higher beat rate (+32bpm) and shorter field potential duration (FPD, -201ms) for Cor.4U. The FPD lengthening after cisapride (100nM: +65% versus +18%), quinidine (10µM: +65% versus +31%), sotalol (30µM: +90% versus +47%) or flecainide (3µM: +76% versus +22%) application appeared earlier in iCell2 as compared to Cor.4U. Arrhythmia occurrence also appeared earlier in iCell2 as compared to Cor.4U for the 3 substances mentioned above. The FPD shortening recorded after verapamil or nifedipine application was similar in both hiPSC-CMs. In conclusion, Cor.4U and iCell2 hiPSC-CMs are both sensitive enough to detect drug-induced delayed or shortened repolarization and arrhythmia and can provide useful predictive cardiac electrophysiology data. Arrhythmias occurred at concentrations higher than clinical free maximum plasma concentrations with an overestimation of the risk with cisapride. However, quantitative differences of baseline electrophysiological characteristics or pharmacological sensitivity of both cell types have to be considered with caution during the interpretation of data. The new chemical entities included within a given drug development program should be evaluated in hiPSC-CMs coming from a single supplier.