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Personalized medicine diagnostics for cardiac safety

Ksenia Blinova

Induced Pluripotent Stem Cell and Electrophysiology Laboratory Office of Science and Engineering Laboratories Center for Devices and Radiological Health US Food and Drug Administration

Personalized medicine uses a diagnostic test to predict which patients will benefit and which are likely to be harmed by therapies. Induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) could potentially be utilized in personalized cardiotoxicity studies, assessing individual proarrhythmic risk. We compared subject - specific iPSC - CMs responses to dofetilide and moxifloxacin with individual clinical responses to the same drugs for a cohort of 16 healthy normal subjects. The delay in iPSC-CMs repolarization and QT interval prolongation induced by these hERG potassium channel blockers were used as surrogate end points of proarrhythmic risk. Comparative results showed no significant correlation between the subject - specific in vitro repolarization prolongation slopes and clinical QT response slopes to either moxifloxacin (P = 0.75) or dofetilide (P = 0.69). Similarly, no significant correlation was found between baseline QT and baseline APD measurements (P = 0.93). This result advances our current understanding of subject - specific iPSC - CMs and facilitates discussion into factors obscuring correlation and considerations for future studies of subject - specific iPSC-CMs assays used to predict individual clinical outcome.