

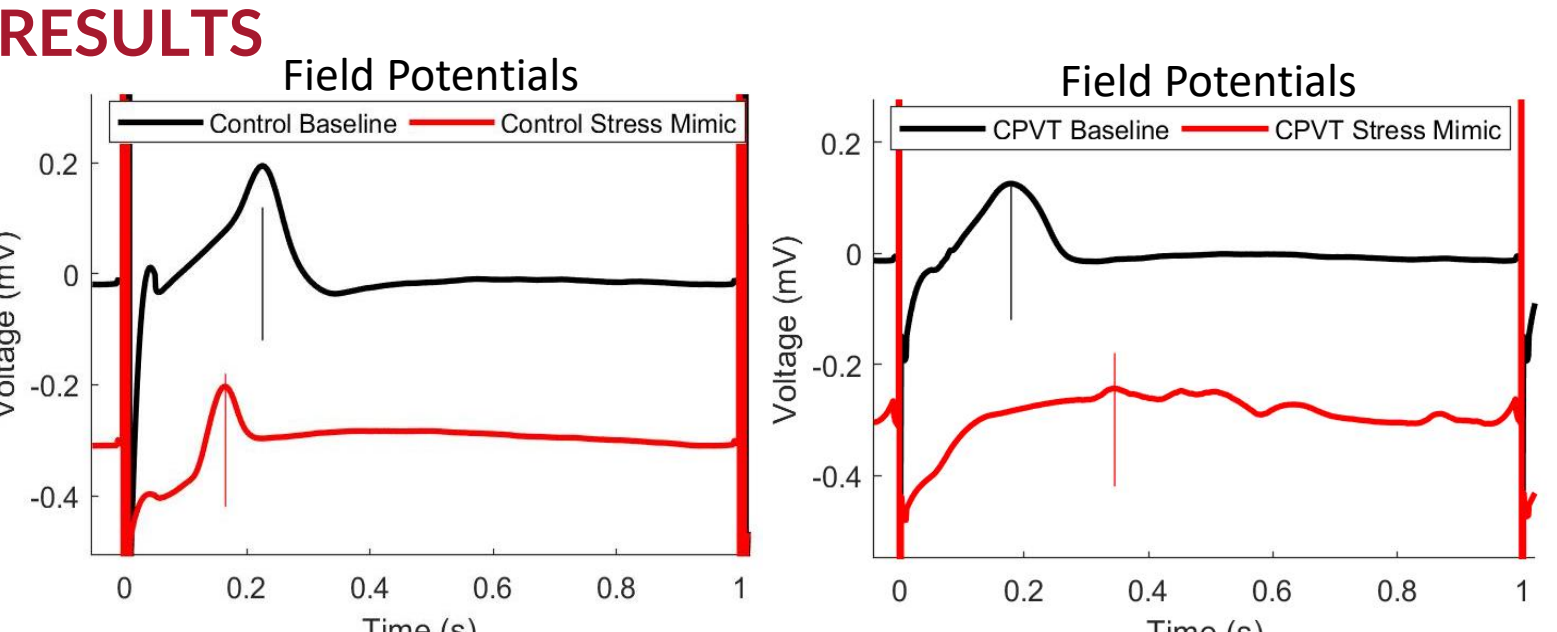
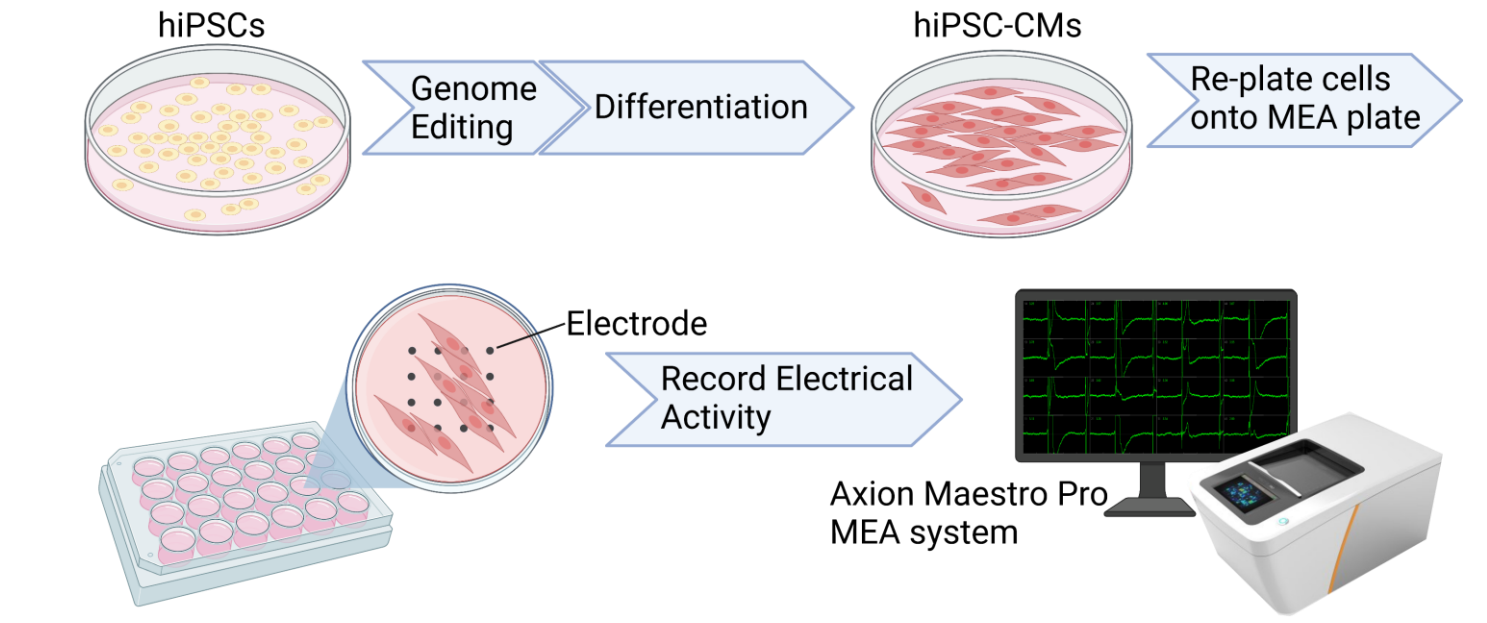
Using Human-Induced Pluripotent Stem Cells to Investigate a Novel CPVT-Related RyR2 Variant

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BACKGROUND Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited cardiac disorder that causes stress/exercise-induced irregular heart beating termed arrhythmia. We investigated a novel cardiac ryanodine receptor (RyR2) variant, R417L.

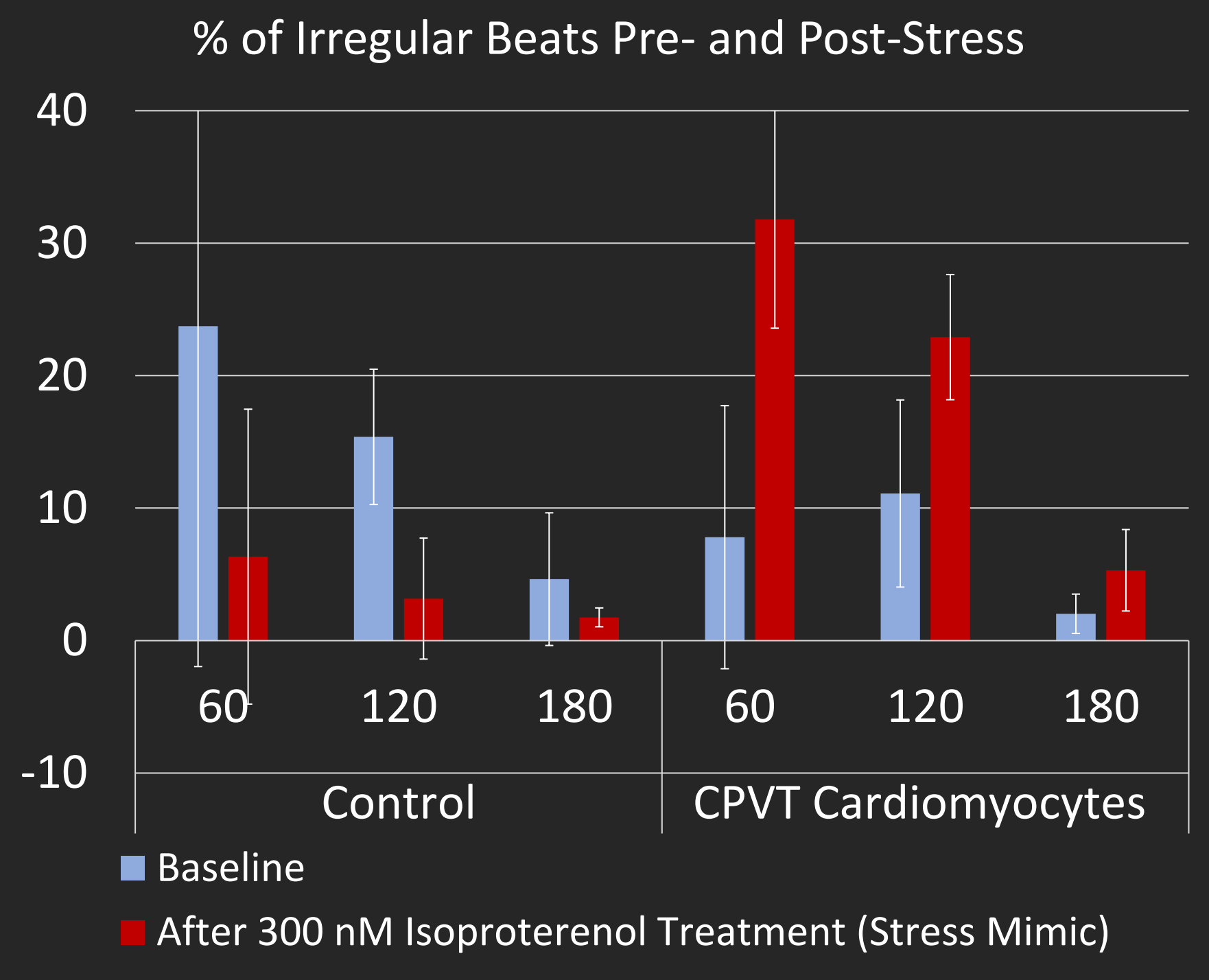
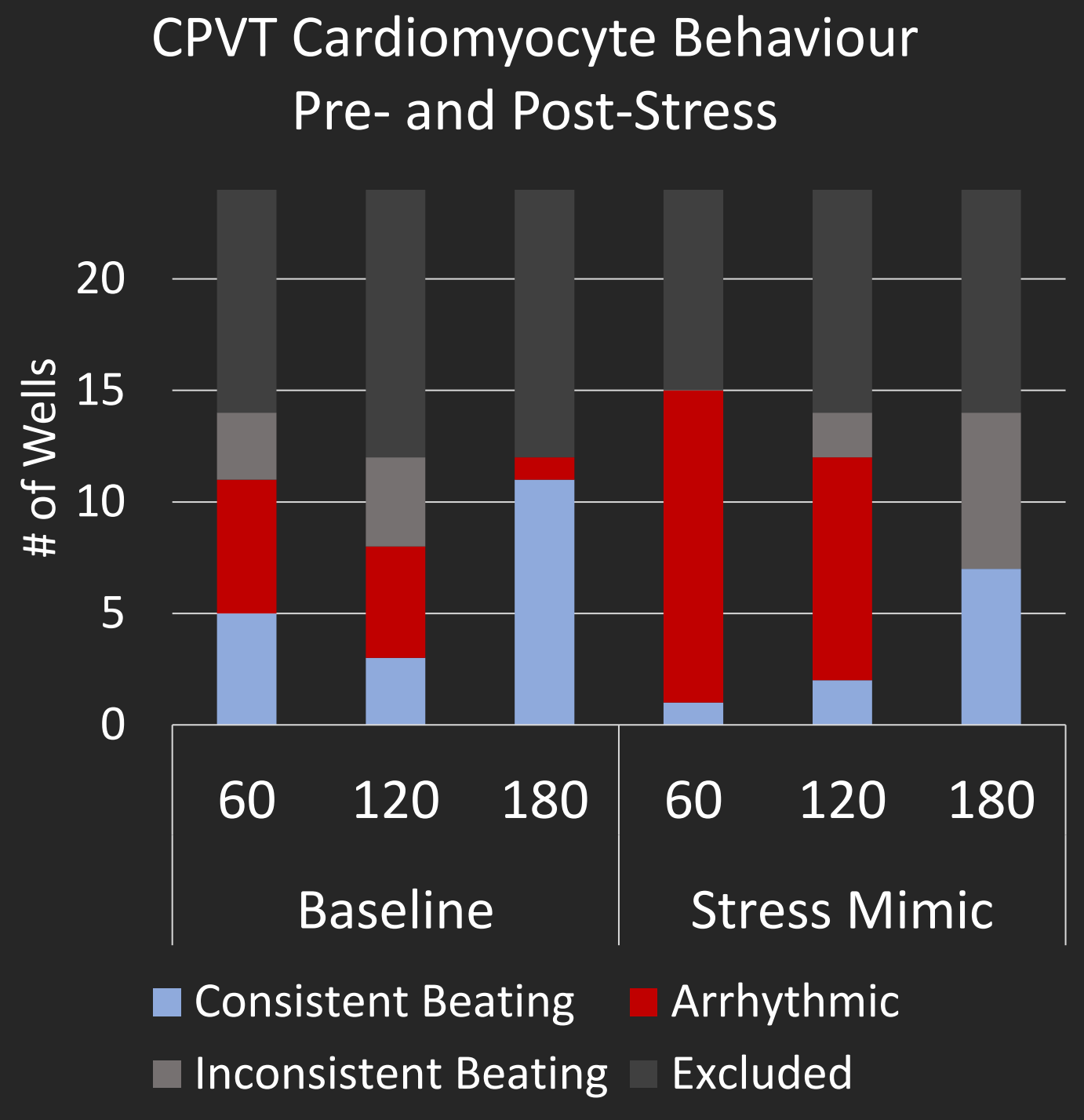
- METHODS**
1. Differentiated human pluripotent stem cells carrying the R417L genetic variant into beating heart cells called cardiomyocytes
 2. Recorded electrical activity from these cells using a microelectrode array (MEA) assay



Control cardiomyocytes (left) display regular electrical activity at baseline (black) and during isoproterenol drug treatment mimicking stress conditions (red). CPVT RyR2 variant cardiomyocytes (right) display regular electrical activity at baseline/rest but exhibit abnormal electrical activity during the stress condition.

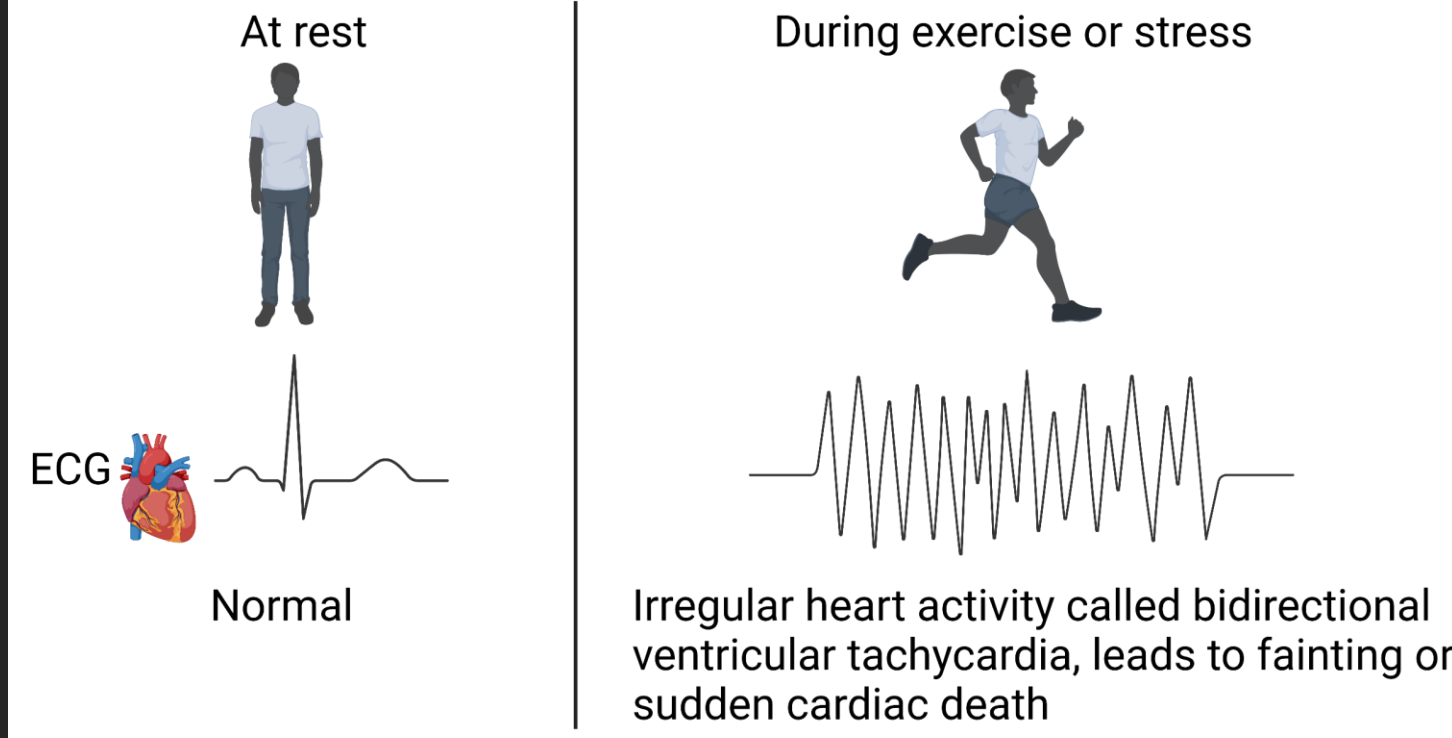
- DISCUSSION**
- First to phenotype the R417L variant in hiPSC-CMs and a pilot for using the MEA to functionally study the CPVT phenotype
 - The R417L variant appears to disrupt normal electrophysiological function of cardiomyocytes under stress conditions
 - Future studies warrant the optimization of the MEA protocol to elucidate further the role of the R417L variant in CPVT

A novel CPVT genetic variant induces electrical instability in cardiomyocytes during stress-like conditions.



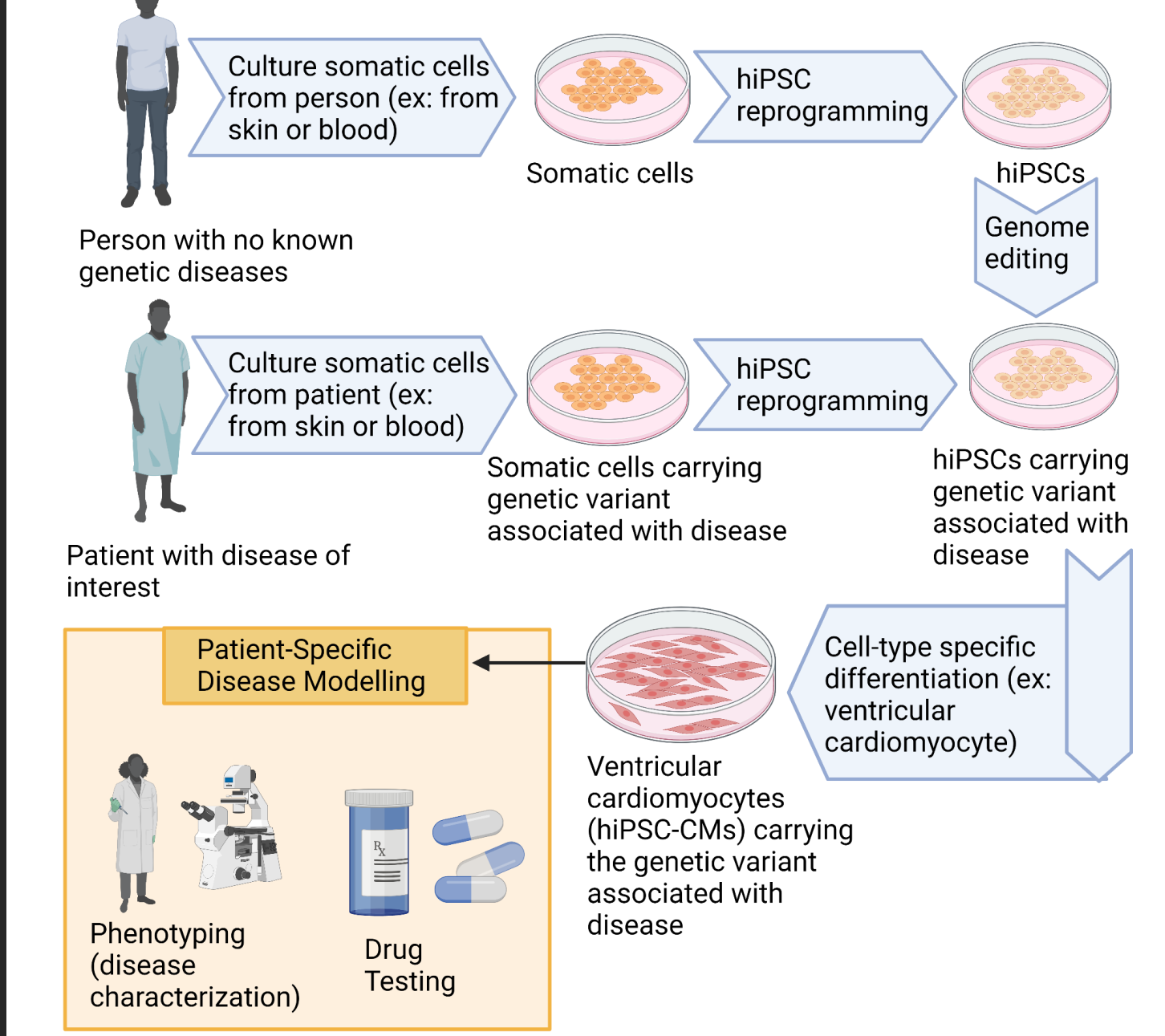
Stress conditions evoked a significant increase in irregular beating among the cardiomyocytes harbouring the CPVT variant but not in the healthy control.

Clinical Manifestation of CPVT



The Cardiac Ryanodine Receptor, RyR2
Calcium release channel that provides the calcium required for contraction of the heart. Most CPVT variants cause excess calcium release/leakage, underlying the ventricular arrhythmia experienced during exercise/stress.

Using hiPSCs for Disease Modeling
Human-induced pluripotent stem cells (hiPSCs) are human cells that have been reprogrammed, rendering them the ability to be differentiated into, meaning turned into, almost any cell type, including beating cardiomyocytes (hiPSC-CMs).



REFERENCES

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