**SUBTY PE-SPECIFIC PROMOTER-DRIVEN ACTION POTENTIAL IMAGING FOR PRECISE DISEASE MODELING AND DRUG TESTING IN HIPSC-DERIVED CARDIOMYOCYTES**

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Cardiomyocytes (CMs) generated from human induced pluripotent stem cells (hiPSCs) are increasingly used in disease modeling and drug evaluation. However, they are typically a heterogeneous mix of ventricular-, atrial- and nodal-like cells based on action potentials (APs) and gene expression. This heterogeneity and the paucity of methods for high-throughput functional phenotyping hinder the full exploitation of their potential. Therefore, to develop a method for rapid, subtype-specific phenotyping of hiPSC-CMs with respect to AP morphology and single-cell arrhythmias, we used cardiac lineage-specific promoters to drive the expression of a voltage-sensitive fluorescent protein, enabling subtype-specific optical AP recordings. In a patient-specific hiPSC model of long-QT syndrome type 1, AP prolongation and frequent early afterdepolarizations were evident in mutant ventricular- and atrial-like, but not in nodal-like hiPSC-CMs compared to their isogenic controls, consistent with the expression of the disease-causing gene. Furthermore, we demonstrate the feasibility of sequentially probing a cell over several days to investigate genetic rescue of the disease phenotype and to discern CM subtype-specific drug effects. Taken together, by combining a genetically-encoded membrane voltage sensor with promoters that drive expression in the major subtypes of hiPSC-CMs, we developed a convenient system for disease modeling and drug evaluation in the relevant cell type that has the potential to advance the emerging utility of hiPSCs in cardiovascular medicine.