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O-373: Non-Invasive Image-Based Assessment of Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes

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Problem: Human induced pluripotent stem (iPS) cells have emerged as a viable source of human cardiomyocytes for developing more accurate in vitro cardiac drug screening platforms. With improved cardiac tissue models, non-invasive, non-destructive methods that assess functional tissue metrics longitudinally in response to drugs are necessary.

Objectives: The objectives of this study are to develop and validate non-invasive and non-destructive methods for assessing the electrophysiology and metabolic state of human induced pluripotent stem cell-derived cardiomyocytes (hiPS-CMs).

Methodology: We differentiated beating hiPS-CM from human iPS cell line WTC-11. The electrophysiological phenotype was assessed using the membrane voltage sensitive dye (VSD), di-4-AN-E(F)PPTEA, and the genetically encoded calcium indicator, GCaMP6. The metabolic phenotype of hiPS-CM was quantified as the ratio of glycolysis to oxidative phosphorylation using fluorescence lifetime imaging microscopy (FLIM) of nicotinamide adenine dinucleotide (NADH), a central metabolite. hiPS-CM were subjected to several stimuli known to affect the metabolism and/or electrophysiology of cardiomyocytes including different doses of isoproterenol, propranolol, hypoxia, and potassium cyanide.

Results: Beta blocker propranolol (10 μ M) and beta adrenergic agonist isoproterenol (100 nM) elicited a 56% decrease and a 19% increase in beat frequency, respectively. 24 hours exposure to hypoxia generated a shift of 17% of pixels analyzed from oxidative phosphorylation to glycolysis ($p = 0.015$). Potassium cyanide (4 mM) generated a significant shift of pixels analyzed from oxidative phosphorylation to glycolysis ($p < 0.05$).

Significance: These unique electrophysiological and metabolic endpoints will facilitate the development of in vitro human cardiac tissues with the potential to identify cardiotoxic effects in drug discovery applications.

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