ARMI SPECIAL SPEAKER 2019

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Engineering Human Heart Chambers and Tissues for Disease Modelling and Drug Discovery

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Abstract

Traditional drug discovery and development is an inefficient and expensive process with unacceptably high failure rates. Although traditional animal models are accessible, major species-specific differences limit their ability to predict human cardiotoxicity, the dominant reason for attrition. To bridge this longstanding gap, we have engineered the world's first 3D electro-mechanically coupled, fluid-ejecting miniature human ventricular cardiac organoid chamber (hvCOC, a.k.a. human heart-in-a-jar), with human pluripotent stem cell-derived ventricular cardiomyocytes (hvCMs) embedded in a collagen-based extracellular matrix, as the only in vitro biomimetic model available in the industry that allows the direct measurement of clinically-relevant, physiologically complex contractile parameters such as ejection fraction, developed pressure, and stroke work, as well as electrophysiological properties including action potential and conduction velocity. Structural characterization showed organized sarcomeres with myofibrillar microstructures, whereas transcript and RNA-seq analyses revealed upregulation of key Ca2+-handling, ion channel, and cardiac-specific proteins in hvCOC compared to lower-order 2D and 3D cultures of the same constituent cells. Furthermore, hvCOC displays key molecular and physiological characteristics of the native human ventricle, shows expected mechanical and electrophysiological responses to a range of pharmacological interventions, and can be readily adapted to iPSC-based disease models (e.g., dilated cardiomyopathy). Together with other human bioengineered cardiac assays including the hvCMs for high-content screening, cardiac anisotropic sheet (hvCAS) for arrhythmogenicity assessment, and cardiac tissue strip (hvCTS) for contractility measurement, the hvCOC completes the comprehensive MyHeart Platform, which provides a unique one-stop, tiered screening approach for next-generation drug discovery, cardiotoxicity screening, disease modeling and other ethnicity-, sex- and patient-specific applications to minimize patient harm and maximize successes. Specific examples of disease models and newly discovered therapeutics will be presented.

CCRM AUSTRALIA Commercializing Living Therapies

EVENT DETAILS

DATE:
Monday, 8th April

TIME:
3:30pm

VENUE:
G19
Ground Floor
15 Innovation Walk
Monash University
Clayton Campus

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