CENIMAT
CENTRO DE INVESTIGAÇÃO DE MATERIAIS

i3N
INSTITUTO DE NANOESTRUTURAS, NANOMODELAÇÃO E NANOFABRICAÇÃO

INVITED SPEAKER

DR. HENRIQUE ALMEIDA

Investigador Senior do IBET

WEBINAR

EXTRACELLULAR MATRIX (ECM) FUNCTIONALIZATION OF HUMAN IPSC-BASED CARDIAC TISSUES IMPROVES CARDIOMYOCYTE MATURATION

Cardiovascular diseases are a leading cause of death and morbidity. Therefore, there is an urgent need to develop new therapeutic approaches targeting this problem. Human induced pluripotent stem cells (hiPSC) have a great potential in developing these novel therapies due to their high self-renewal capability and potential to differentiate into specialized cells, including cardiomyocytes (CM). However, generated hiPSC-derived CM (hiPSC-CM) are still immature. This immaturity has been limiting their application, in vitro cardiac disease modeling, and cardiotoxicity drug screening. Recent findings have demonstrated extracellular matrix (ECM) potential as a key regulator in development, homeostasis, and injury of the in vivo cardiac microenvironment [1]. Within this context, this work's objective was to assess the impact of human cardiac ECM biomaterial in the phenotype, functionality, and maturation of hiPSC-CM.

Human ECM was isolated from the myocardium through physical decellularization. The ECM was polled and cryomilled and further characterized for particle size and composition. These ECM particles were then incorporated in a 3D model of hiPSC-CM[2] and cultured as aggregates in dynamic stirred culture. hiPSC-CM were characterized in terms of phenotype, structure, and functionality after two weeks of culture.

Our results showed that the cardiac tissue decellularization process reduced DNA content and maintained ECM composition. SEM and AFM characterization indicated that tissue cryomilling breaks down tissue into micrometric-sized particles with a spherical-like shape and irregular surface topography. The Cardiac ECM particles were successfully incorporated in 3D hiPSC-CM aggregates, with no impact on cell morphology, aggregate size, composition, and metabolic activity. ECM biomaterial aggregates showed beating rates closer to physiologic values, more organized and longer sarcomeres, and improved calcium handling when compared to standard hiPSC-CM aggregates.

This work shows for the first time that human cardiac ECM biomaterial promotes the structural and functional maturation of hiPSC-CM. The knowledge generated provides essential insights to strengthen the application of ECM and hiPSC-CM in cell therapy, drug discovery, and cardiac disease modeling.

References:

[1] A. H. Fong, M. Romero-López, C. M. Heylman, M. Keating, D. Tran, A. Sobrino, A. Q. Tran, H. H. Pham, C. Fimbres, P. D. Gershon, et al., Tissue Eng. Part A 2016, 22, 1016.

[2] C. Correia, A. Koshkin, P. Duarte, D. Hu, M. Carido, M. J. Sebastião, P. Gomes-Alves, D. A. Elliott, I. J. Domian, A. P. Teixeira, et al., Biotechnol. Bioeng. 2018, 115, 630.

09TH

APRIL, 2021
01:30 P.M.

CLICK HERE TO ACCESS ZOOM

UNIVERSIDADE NOVA DE LISBOA
OMNIS CIVITAS CONTRA SE DIVISA NON STABIT

NOVA SCHOOL OF SCIENCE & TECHNOLOGY