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DECELLULARIZED EXTRACELLULAR VENTRICULAR PORCINE HEART MATRIX LEADS TO IMPROVED STRUCTURAL ARRANGEMENT AND DEVELOPMENT OF HUMAN IPS CELL-DERIVED CARDIOMYOCYTES AND FIBROBLASTS

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The purpose of this investigation was to determine the effect of decellularized extracellular porcine heart matrix (ECM) on the transcriptional and structural properties of cardiomyocytes in culture. Cardiomyocytes from induced Pluripotent Stem (iPS) cells were plated at a progenitor and differentiated state onto an ECM. The ECMs were compared against a monolayer control condition grown on vitronectin-coated plates. The structural differences between all three conditions was carried out using confocal microscopy. The monolayer condition was shown to have random structure of CMS with fibroblasts sporadically dispersed throughout the sample. Progenitor plated cells revealed CMs that formed fiber-like structures with specific directionality and interweaved with fibroblasts throughout. Differentiated plated cells showed three-dimensional structure of CMs, with a general directionality, however this did not show directed growth, nor close interaction with fibroblasts. Further comparison was performed between the monolayer plated condition and the progenitor plated condition through use of single-cell RNA sequencing. Pathways related to upregulated genes of CMs cultured on the ECM were related to cardiac structure and contraction. Fibroblasts cultured on ECM showed upregulation in genes related to sustaining CM function, thereby coinciding with one of their main purposes within the heart. Through these modes of analysis, it is evident that progenitor plated CMs on ECM produce superior results than the other culturing conditions. The fiber-like structures of CMs and upregulation of pathways related to native CM and fibroblast function in the heart allow for an improved cardiac model that can be used to study and treat diseases.