Tissue Engineering Model to Study Mitral Annulus Calcification under Diabetic Conditions

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The mitral valve (MV) is located between the left atrium and left ventricle, and its main function is to allow unidirectional blood flow through the heart. There are four major components of the MV: annulus, leaflets, chordae tendineae, and papillary muscles[1]. The annulus is a fibrous, saddle-shaped "ring" that can contract and relax with the myocardium[1]. Mitral annulus calcification (MAC) is a chronic degeneration of the fibrous structure in the MV[2]. The prevalence of MAC is around 15% but increases in patients with other cardiovascular diseases and risk factors[2]. The prevalence of MAC is also thought to be higher in patients with type 2 diabetes (T2DM), but MAC has not been properly characterized within this population because of confounding factors such as cardiac disease[3].

There are two main types of cells present in the MV: valvular endothelial cells (VECs) and valvular interstitial cells (VICs)[4]. VICs can be found throughout the ECM of the MV and are thought to maintain the structure of the valve, and the entire MV is covered in VECs[4]. VECs and VICs have been shown to communicate with each other in order to regulate their phenotypes[4].

The goal of this project is to reveal the interactions between the mitral valve annular cells (VECs and VICs) that lead to calcification under reproducible bioreactor conditions. These cells will be cultured and observed under static and dynamic conditions, and each cell type will be cultured under normal glucose concentrations and high glucose concentrations. A Flexcell compression system will be used for dynamic cell culture. We will run a MV bioreactor with a porcine MV that has been decellularized and seeded with both VICs and VECs. Immunofluorescence and Western Blot analyses will be performed on samples from the static and dynamic cell culture as well as the bioreactor. Our proteins of interest include osteocalcin, α-Smooth Muscle Actin (αSMA), E-selectin, and glycated proteins.

References:

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