Grafting 3D Collagen Scaffolds onto Infarcted Myocardium Improves Cardiac Remodelling and Neo-angiogenesis

This study aims to investigate the influence of myocardial microenvironment, mass transfer properties, and stiffness of the grafted collagen scaffolds in cardiac cell behavior and function, in cardiac remodeling processes. The ultimate clinical goal is to develop a grafting technique to inoculate ECM-like matrices on to the heart in patients with acute myocardial infarction (MI).

Figure 1. (A) Schematic representation of the neovascularization of myocardial infarction (MI) with 3D collagen scaffold. The neo-vascularization within the scaffold that prevents the spread of fibrosis and the risk of coronary stenosis (reproduced from Gabcík et al., J Heart Lung Transplant 2006). The process of scaffold degradation and neo-vascularization is critical in modulating the differentiation of the hematopoietic cells and in the cardiac function.

Experimental Methods: In vitro reconstituted type I collagen gel. Compression by applying different compression stresses for 2 minutes, in order to produce dense, multi-layered scaffolds with improved mechanical properties. Mouse models of MI will be produced using left anterior descending artery ligation immediately after infusion. The scaffold will be infused into the injured myocardium along the coronary microcirculation. Post-operative results will be compared with sham-operated controls. Vascularization, neovascularization, and basement membrane thickness will be measured. The ability of the Scaffold to enhance cardiac function will be assessed using treadmill exercise and echocardiographic analysis. The scaffold will be biodegradable, allowing for integration into the myocardium.

Stretch Regulated Response of the Notch Pathway in EMCs

Cardiovascular disease (CVD) is one of the most prevalent killers in the United States, increasing prevalence coupled with an aging population has underscored the need for novel therapies and clinical approaches to CVD disease. Congestive heart disease, affecting nearly 1 out of every 3000 Americans, is the leading cause of heart disease and a significant cause of morbidity and mortality. The Notch/CAD program represents a new therapeutic strategy for treating this disease. By targeting the Notch pathway in EMCs, we can further our understanding of the disease and potentially develop novel therapies.

Experimental Methods: We have used an ACS to analyze epicardial tumors based on the location of the Nkx2-5 and the SU5402 repressor. The strategy is to use a reporter gene to monitor the expression of the Nkx2-5 gene in the tumors. This allows us to study the development of the tumors and to identify potential therapeutic targets.

Epidermal Specific Rainbow-Cre mouse

Current existing tools to analyze epicardial tumors based on the location of the Nkx2-5 and the SU5402 repressor. We have proposed generating a Rainbow-Cre mouse that will allow the fine-tuning of the gene expression and therapeutic methods occurring during epicardial differentiation and map individual cell lineages.

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Figure 2. Confocal laser scanning microscopy of collagen-encapsulated A549 cells (A) and collagen-encapsulated human mesenchymal stem cells (B) cultured for 24 hours. The cells were stained with calcein AM (green) and propidium iodide (red). The images were acquired using a confocal microscope and analyzed using ImageJ software. The results show that the scaffolds support cell viability and proliferation in vitro.

Figure 3. Cyclic Stretching Response of Epicardial Mesenchymal Cells. Using a fixed cell-cell stretching apparatus, images of the cells were acquired during stretching cycles. The cells were stained with calcein AM and analyzed using ImageJ software. The results show that the cells maintain their viability and proliferation during stretching.

Figure 4. Laser scanning confocal images of A549 cells stained with TRITC- and FITC-conjugated secondary antibodies (A) and stained with DAPI and Sytox Green (B). The images were acquired using a confocal microscope and analyzed using ImageJ software. The results show that the scaffolds support cell viability and proliferation in vitro.