Endothelial Differentiation of c-kit+ Cardiac Progenitor Cells in Extracellular Matrix-Fibrin Hybrid Hydrogel Scaffolds

Budina, Erica

Congenital heart defects are the leading cause of death in infants and young children. Current surgical procedures are unable to replicate the anatomy and function of the native myocardium. This study aims to develop a biomimetic scaffold which recapitulates the biochemical and mechanical cues of cardiac tissue. An important challenge is the implementation of intrinsic vascularity and transport systems needed to nourish the engineered tissues. In phase 1, solubilized cardiac extracellular-matrix and fibrin were cross-linked via transglutaminase (TG) to create a hybrid scaffold with tunable stiffness. Increasing the concentration of TG from 0 to 120 μg/ml increased the Young's Modulus from 2.07 kPa to 29.70 kPa, resulting in scaffolds whose stiffness spanned the range of the developing and mature myocardium. Cell viability was not significantly affected by increasing the cross-linker. In phase 2, c-kit+ cardiac progenitor cells (CPCs) were seeded in the scaffolds and their differentiation into endothelial cells was investigated. It was hypothesized that tuning the stiffness of the scaffold to mimic that of the native myocardium would enhance the differentiation of CPCs into endothelial cells. Results of the DNA assay showed that proliferation, a characteristic of stem cells, decreased with increasing stiffness after 12 days. Real Time Quantitative PCR analysis indicated up-regulation of the VWF gene (a marker for endothelial cells) in stiffer formulations, which suggests greater endothelial cell differentiation. The findings of this study are an important step toward the development of a biomimetic scaffold which promotes endothelial differentiation of CPCs and consequently of intrinsic vascularity in ECM-fibrin hybrid scaffolds.

Awards Won: