Decellularized and Vascularized Scaffolds for Tissue-Engineered Regeneration of Myocardium

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Introduction

Myocardial infarction (MI) affects nearly 1,000,000 individuals each year, and the resulting damage initiates a pathological progression toward congestive heart failure (CHF)\(^1\). In order to forestall CHF, tissue engineering therapies must target replacement of the infarct scar with functional cardiac muscle\(^2,3\). Long-term in vivo functionality of thicker (> 200 µm) tissue engineered grafts has been hindered by insufficient graft vascularization\(^3\). Thus, there is a great need for thick, acellular, fully vascularized, and biocompatible myocardial scaffolds that provide agreeable biological “niches” for regenerative cells in both in vitro and in vivo applications of myocardial tissue engineering.

Materials and Methods

We generated decellularized myocardial flap scaffolds comprising porcine left-ventricular myocardium and its associated coronary arteries and veins by perfusing the vasculature with sodium dodecyl sulfate (SDS) and/or sodium hydroxide (NaOH). The effects of these reagents upon the myocardial extracellular matrix (ECM) and the vascular ECM were compared through histology, immunohistochemistry, mechanical testing, and quantitative assays for collagen, elastin, and DNA content. Corrosion casting and fluorescent dye injection were used to demonstrate the integrity of the vasculature. To assess cytocompatibility, scaffolds were seeded with cardiac cells and stained for cell viability and cardiomyocyte-specific markers\(^4\).

Results

All scaffolds displayed a fully intact and patent vasculature with arterial burst pressures indistinguishable from native coronary arteries and perfusion to the level of capillaries. Scaffolds were devoid of cellular proteins, contained only residual DNA, retained collagen and elastin ECM components, exhibited excellent mechanical properties, and were compatible with seeded cells. SDS perfusion preserved collagen IV, laminin, and fibronectin well, while NaOH significantly reduced levels of laminin and fibronectin\(^4\).

Discussion and Conclusions

Perfusion of tissues with SDS, NaOH, or both is a viable approach for generating acellular, vascularized scaffolds. Scaffolds retain the composition and architecture of the myocardial and vascular ECM. In the future, scaffolds could be seeded with appropriate cell types, and, upon implantation, may be able to functionally integrate within host myocardium and be nourished by direct anastomotic connection to the host’s own vasculature. Our seeded scaffolds might also be used as physiologically accurate models for in vitro studies of cardiac physiology and pathology and to identify new therapies and drugs.

References


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Disclosures

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