Electrospun elastin-like polypeptide enriched polyurethanes and their interactions with vascular smooth muscle cells

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A B S T R A C T

In vascular tissue, elastin is an essential extracellular matrix protein that plays an important biomechanical and biological signalling role. Native elastin is insoluble and is difficult to extract from tissues, which results in its relatively rare use for the fabrication of vascular tissue engineering scaffolds. Recombinant elastin-like polypeptide-4 (ELP4), which mimics the structure and function of native tropoelastin, represents a practical alternative to the native elastic fibre for vascular applications. In this study, electrospinning was utilized to fabricate fibrous scaffolds which were subsequently surface modified with ELP4 and used as substrates for smooth muscle cell culture. ELP4 surface modified materials demonstrated enhanced smooth muscle cell (SMC) adhesion and maintenance of cell numbers over a 1-week period relative to controls. SMCs seeded on the ELP4 surface modified materials were also shown to exhibit the cell morphology and biological markers of a contractile phenotype including a spindle-like morphology, actin filament organization and smooth muscle myosin heavy chain expression. Competitive inhibition experiments demonstrated that the elastin–laminin cell surface receptor and its affinity for the VGVAPG peptide sequence in ELP4 molecules are likely involved in the initial SMC contact with the ELP4 modified materials. Elastin-like polypeptides show promise as surface modifiers for candidate scaffolds for engineering contractile vascular tissues.

1. Introduction

Cardiovascular diseases, such as atherosclerosis and coronary arterial restenosis, are the leading cause of morbidity and mortality in the developed world [1]. These disorders are characterized by a phenotypic modulation of smooth muscle cells (SMCs) from their quiescent contractile phenotype to a more proliferative state [2]. This is accompanied by an increase in cell migration from the vascular media into the arterial lumen, resulting in neo-intima formation and arterial occlusion; a pathology known as neo-intimal hyperplasia. Vascular tissue engineering approaches have the potential to provide substitute vessels to replace diseased ones through the use of cells, scaffolds and bioactive stimuli to control the degree of SMC proliferation and migration into the arterial lumen. Scaffold materials which provide appropriate biological signals are thus an important aspect of vascular graft tissue engineering.

Biomimetic materials can exploit the structural and biological design of the extracellular matrix (ECM) environment that has been optimized through the evolutionary process. In the vascular media, elastin is an ECM protein present in high abundance and can account for up to 50% of a blood vessel’s dry weight [3]. Li et al. demonstrated the importance of elastin through studies with elastin deficient knockout mice, whereby they showed that the elastin-null subjects exhibited early mortality in postnatal life due to excessive subendothelial SMC proliferation and accumulation, resulting in arterial occlusion [4]. Traditionally, elastin’s role in the arterial wall was believed to be solely biomechanical in nature, providing the elasticity necessary to withstand the pulsatile hemodynamic forces of blood perfusion; however, there is growing evidence that the elastin protein may also play an important role in controlling SMC activity through biological signalling [5]. Karnik et al. have demonstrated the effect of tropoelastin, elastin and elastin-derived peptides on smooth muscle cell activity and further identified the importance of the VGVAPG amino acid repeat sequence in this cell response [6,7].

While elastin plays an important role in the vascular media, to date, it has not been extensively utilized in the design of vascular tissue engineering scaffolds. Native elastin is insoluble due to its...