Surface modification of electrospun nanofibers via blending: Controlling hydrophobicity/hydrophilicity for protein adsorption

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Statement of Purpose/Introduction: Regeneration of a tissue in-vitro/in-vivo often requires an artificial extracellular matrix (ECM) that has a three-dimensional (3D) architecture. These structures, commonly referred to as scaffolds, are of central importance in most tissue engineering strategies. Since most tissue types are made up of an ECM that is fibrous in nature, a biomimetic approach for scaffold synthesis would entail the synthesis of a fibrous matrix [1]. Another important aspect of the native ECM fibers is that their diameters span from few nanometers (tropocollagen unit) to tens of microns (collagen fiber bundle) [2]. However, it has been recently demonstrated that fibers having diameters in the nanometer range elicit a favorable response by cells [3]. Therefore, in this study we synthesized electrospun nanofibers using an FDA approved polymer poly(lactide-co-glycolide) (PLGA). However, the hydrophobicity of PLGA can lead to enhanced interaction / increased spreading of proteins, that can adversely affect protein conformation and as a consequence, protein delivery applications for tissue engineering [4]. Therefore, it would be useful to provide controlled hydrophilicity to these hydrophobic nanofibers to make them more suitable as scaffolds for growth factor delivery in tissue engineering and other biomedical applications.

In this study, we report the synthesis of nanofibers of a novel blend of PLGA with a tri-block copolymer - poly(ethylene glycol)-poly(propylene glycol)-poly(ethylene glycol) (EPE) which imparts controlled hydrophilicity (dependant on percent content) while maintaining the desirable properties of the hydrophobic PLGA nanofibers such as biocompatibility, biodegradablility, and spinnability.

Methods: Blends of PLGA (85:15 - Mw 45000-70000) / PLGA (75:25 - Mw 90,000-126,000) with varying content of EPE (Mn 14,600) were electrospun into nanofibers. The surface morphology and diameter of nanofibrous scaffolds were characterized by scanning electron microscopy (SEM) and porosity was measured by mercury porosimetry. The hydrophilicity/surface energy of the nanofibrous scaffolds was characterized using a contact angle measuring goniometer. Atomic force microscopy (AFM - phase imaging) was used to detect the presence of EPE on the surface of the electrospun blends. Chemical characterization and potential polymer chain interactions between blended polymers were studied using fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR). For potential growth factor delivery applications, protein adsorption and release was conducted

Result/Discussion: Electrospun blends of PLGA (22-20% w/v) with EPE (0.5-2% w/w) produced nanofibers ranging from 200-800 nm in diameter. The contact angle measurement of nanofibrous matrices demonstrated that the incorporation of EPE from 0.5-2.0 % w/w enabled a significant change in hydrophobicity (**Figure: 1**).

These results prompted a surface analysis (AFM non contact mode) of the nanofibers to determine the presence of EPE on nanofiber surfaces. The surface analysis revealed no phase change (data available but not shown) in the blended nanofibers, thereby indicating that the surface probably has only PLGA (single constituent) as EPE is blended in rather small percentages (0.5-2.0 % w/w). A major consequence of blending / decrease in hydrophobicity could be enhanced adsorption of proteins. To study the influence of blending on protein adsorption and release, a model protein bovine serum albumin (BSA) was used.
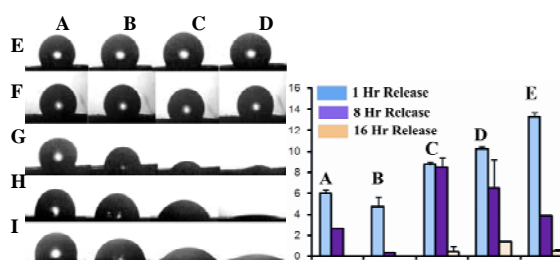

Figure 1: Contact Angle Video snapshots of a water droplet on nanofibrous matrices. **Column: A**:16th frame/1sec, **B**:26th frame/1sec, **C**:56th frame/1sec, **D**:16th frame/2sec, **Row: E**:pure PLGA, **F**:EPE0.5%, **G**:EPE1%, **H**:EPE1.5%, **I**:EPE2%.

Figure 2: BSA protein release studies from nanofibrous matrices. **Y** axis; Amount of protein released (μg/ml) **A**: Pure PLGA, Blended PLGA matrices (B-E) **B** 0.5% EPE, **C**: 1% EPE, **D**: 1.5% EPE, **E**: 2% EPE

The release profile of a model protein BSA demonstrated improved adsorption (10-40%) on 1.0 - 2.0 % EPE blended PLGA nanofibers with 1.0 and 1.5 % EPE blended nanofibers showing better sustained release profiles for 36 hr. (**Figure: 2**) These results demonstrated that purely hydrophobic and purely hydrophilic materials may not be suitable for enhanced adsorption / release of proteins. However, controlled hydrophobicity/hydrophilicity is probably a better choice for enhanced protein adsorption / release. Further, FTIR and NMR analysis revealed the presence of inter-polymeric chain interaction between PLGA and EPE which could be speculated as the reason for change in conformation (data available but not reported) and as a consequence change in physical properties of the blended nanofibrous system.

Conclusion: These studies demonstrated that blending PLGA with small quantities of EPE (0.5-2.0 % w/w) can enable control on the surface properties of electrospun nanofibrous scaffolds. This control on the hydrophobicity / hydrophilicity in turn influences protein adsorption and release that can be of importance in tissue engineering applications.

References:
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