Application of Electrospinning to Produce Hybrid Nanofibrous Scaffolds for Tissue Engineering

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Statement of Purpose: The uniqueness of this project lies in developing a biodegradable core-sheath bicomponent nanofiber scaffold for tissue engineering. Scaffolds containing nanofiber structures are shown to simulate the native environment of the tissues [1], and the electrospinning technique has emerged as the method of choice for developing such structures [2,3].

The polymers proposed for the study are the natural polymers (collagen and gelatin) for the sheath and the synthetic polymer, polycaprolactone (PCL), for the core. The natural polymer is biocompatible and has the inherent capability for binding cells, owing to the presence of cell recognition compounds [4]. The natural polymer, however, lacks strength and degrades too rapidly for the tissue to develop adequately. The synthetic polymer, on the other hand, is not as biocompatible but has the necessarily required mechanical properties (strength) and its degradation rate can be controlled effectively [5]. The sheath-core arrangement, with both polymers biodegrading but the sheath degrading faster and core more slowly, provides the best combination. It is hypothesized that the natural polymer sheath will initiate and aid in cell adhesion & proliferation and then degrade whereas the core will provide the required mechanical integrity for further development of the tissue and then itself be resorbed. This will, as envisioned, leave a 3-dimensional tissue ready for implantation.

Methods: A novel 'co-axial electrospinning' system was set up. The polymers selected were collagen (type I) and gelatin, for the sheath and PCL for the core. The solvent used for gelatin-PCL spinning was glacial acetic acid and that for Collagen-PCL was 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP). Effects of polymer concentration, feeding rate, and applied voltage, on morphology of the scaffold were investigated. In vitro degradation rates of the polymers in PBS solution (at pH 7.4 & 37^{o}C) were examined. The structure of the bicomponent scaffold was characterized using SEM and TEM. To examine the core-sheath morphology, cross-sectioning and freeze-fracturing methods were adopted.

Results/Discussion: Core-sheath structures using PCL-gelatin and PCL-collagen were successfully developed as demonstrated by the electron microscopy techniques (Fig. 1). The fibers produced were also of nano dimensions [Fig. 2]. It was found that the core-sheath structure was formed only at a critical voltage. Values below or above this caused either the polymers to drip or the two polymers to produce separate fibers.

Feeding rates used for the polymers showed a positive effect on the fiber diameter: diameter increased with feeding rate. Similarly, the concentration of polymer in solution had a direct effect on the size suggesting that the core and sheath dimensions increased with concentration.

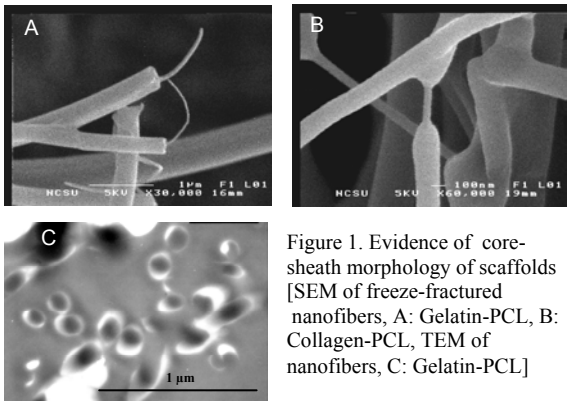

Figure 1. Evidence of core-sheath morphology of scaffolds [SEM of freeze-fractured nanofibers, A: Gelatin-PCL, B: Collagen-PCL, TEM of nanofibers, C: Gelatin-PCL]

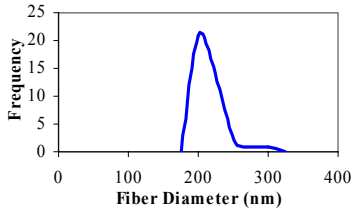

Figure 2. Diameter distribution of Gelatin/PCL fibers

In-vitro hydrolytic degradation study demonstrated that the degradation rate of PCL nanofibers was very low since no apparent change in the fiber morphology was observed even after 1 month in PBS. On the other hand, Collagen disintegrated within a few hours in PBS. To decrease its degradation rate, collagen was cross-linked with glutaraldehyde vapors for 1 day. It was found that cross-linking slowed down the degradation rate of collagen.

Conclusions: This study shows that core-sheath nanofiber scaffolds can be successfully constructed using electrospinning technique. The dimensions of the fibers can be controlled using different feeding rates and polymer solution concentrations. Results of in-vitro degradation studies support the hypothesis in that collagen degrades faster than PCL, and its degradation rate can be controlled to some degree using cross-linking techniques.

Current Studies: Cell-culture studies using human mesenchymal stem cells (hMSCs) are in progress to evaluate the viability of the collagen/ PCL scaffolds for tissue engineering.

References:

1. Smith LA, Colloids & Surfaces, 2004; 39:125-131
2. Yashimoto *et al.*, Biomaterials 2003;24(12):2077-2082
3. Wnek *et al.*, Nano Lett. 2003;3(2):213-216
4. Boland *et al.*, Front. Biosci. 2004;9:1422-1432
5. Hakkarainen, Adv. Polym. Sci. 2002;157:113-138