Gradient Nanofiber Scaffold Libraries for Rapid Screening of Cell-Material Interactions

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Introduction: Scaffolds play a key role in tissue engineering wherein they provide structural support for cells to adhere, grow and guide them to synthesize tissue. Scaffolds made of multiple biomaterials are typically required to mimic the structural and compositional features of native extracellular matrix. Screening the effect of scaffold compositions and properties that optimize tissue regeneration is the key for the selection of scaffolds for use in tissue engineering. Although previous approaches for rapid screening have used biomaterial libraries in the form of two-dimensional (2D) surfaces or films, biomaterials are commonly used in a 3D scaffold format and cells behave more physiologically when cultured in a 3D-matrix environment. Therefore, we report a new combinatorial electrospinning technique for the production of well-defined continuous-gradient nanofiber scaffold libraries suitable for rapid screening cellular responses such as adhesion, proliferation and differentiation that optimize tissue regeneration.

Methods: A two spinneret approach has been developed to fabricate the libraries which consisted of non-woven mats of nanofibers containing a gradient in nanofiber composition. The processing condition of fabricating gradient nanofiber scaffold libraries was optimized by controlling the polymer solution parameters, such as polymer relative molecular mass (Mw), viscosity, surface tension, conductivity, and the process parameters, such as solution flow rate, electric potential, distance between spinneret and collector, etc. Poly(ε-caprolactone) (Mw 80,000) (PCL) was used to fabricate scaffold libraries using 10 % mass/volume solutions in 3:1 chloroform:methanol. In order to characterize the composition of the gradient scaffold libraries, a colored dye (Sudan IV) was incorporated into one of the polymer solutions and nanofiber libraries with gradients in dyes were electrospun. Dye absorbance was measured using a plate reader to characterize composition quantitatively. Next, nanofiber libraries with a gradient in hydroxyapatite nanoparticles (nHA) were fabricated similarly using PCL-nHA solution (30 % nHA by mass) so that the effect of nHA composition on cell response could be screened. nHA was chosen because it is known to enhance osteoblast differentiation and osteogenesis. The libraries enable screening of many nanofiber scaffold compositions and associated properties with a single scaffold specimen.

Results: A nanofiber scaffold library with a gradient in sudan IV (red dye) is shown in Fig. 1a. Dye absorbance measurements showed that a linear gradient in nanofiber composition can be attained with the 2-spinneret approach (Fig. 1b). Red dye gradients are useful for characterizing fabrication feasibility, but gradients in hydroxyapatite nanoparticle composition are fabricated for screening cell response. Images of control nanofiber scaffolds containing nHA are shown in Fig. 2. Thermogravimetric analysis was used to demonstrate that the nanofiber mats contained linear gradients in nHA composition. The nHA scaffold libraries will be utilized to screen the cellular responses in vitro.
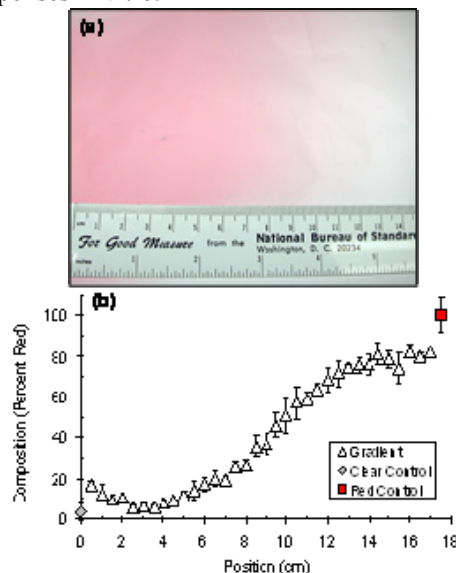

Fig. 1. (a) Photograph of a nanofiber scaffold library. red dye was used to visualize the gradient. (b) Plot of red dye composition versus library positions (n=5). Error bars are standard deviation which is the same as the combined standard uncertainty for the purposes of this work.
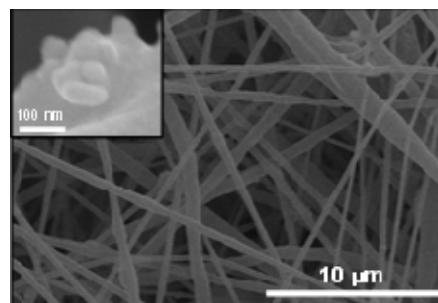

Fig. 2. SEM of electrospun nanofibers contanining 30 % by mass nHA. Inset shows a close-up of nHA of the surface of a nanofiber.

Conclusions: A novel approach has been developed for fabricating nanofiber scaffold composition gradients. The gradients can be used as "libraries" for screening the effect of nanofiber compositions and properties on cell response that optimize tissue regeneration.

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