Gradient Nanofiber Scaffold Libraries for Tissue Regeneration by Electrospinning

Functional tissue engineering is a rapidly emerging biomedical field that holds great potential for healthcare in addressing the gap between need and availability of donor tissues and organs. The goal in the field of tissue engineering is to harvest a biopsy of cells from a patient, seed them on a scaffold to culture a replacement tissue and transplant the cultured tissue into the defective site. One approach for fabricating tissue scaffolds is electrospinning.

Electrospinning employs electrostatic forces to produce well-defined polymer fibers, ranging in diameter from a few micrometers down to tens of nanometers, which can be used as scaffolds for tissue generation. The merit of nanofiber scaffolds for tissue engineering is that they mimic the structural morphology of native extracellular matrix (ECM). Cells in vivo exist within an ECM which is composed of nanoscale fibers made of proteins such as collagen. Cell behavior is more physiological during culture in electrospun scaffolds because the scaffolds mimic this nanofibrous structure of native ECM.

Electrospinning consists of three major components: the spinneret, the fiber collector and the power source. For the spinneret, a polymer solution is pumped from a syringe through a metal needle. The fiber collector is a conductive surface (aluminum foil). Finally, a voltage is applied across the spinneret and the fiber collector for the conversion of polymer solution into a charged jet as it is pumped from the spinneret. The charged jet is very thin which allows the solvent to rapidly evaporate resulting in the formation of a very thin polymer nanofiber. The polymer nanofibers deposit on the collector into a non-woven mat. This non-woven mat serves as a scaffold substrate for tissue generation.

For many tissue engineering applications, in particular bone tissue engineering, multiphase scaffolds made of multiple biomaterials are typically required. Properties from the different material components are combined to yield more effective scaffolds. Thus, we have developed an approach for applying the “multiphase” principle to electrospun nanofiber scaffolds. Two spinnerets are employed for simultaneous deposition of two different polymer solutions into a non-woven mat composed of a mix of the two nanofiber types (patent pending). In addition, the co-deposition yields a nanofiber scaffold containing a gradient in nanofiber composition which can be used as a “library” for high-throughput screening of cellular response of the multiphase nanofiber scaffolds (Fig. A).

Fig. A is a photograph of a nanofiber library made from the biocompatible polymer poly(caprolactone) (PCL). The two spinnerets both pump PCL solutions but one syringe contains a PCL solution with a red dye and the other syringe contains a PCL solution with a blue dye. The addition of the red and blue dyes makes the gradient in nanofiber composition visible to the eye. As can be seen in Fig. A the scaffold library has three different color regions produced as a result of the two different dyes being used in the experiment: (i) a red nanofiber region on left, (ii) a purple region in the middle composed of a mix of red and blue nanofibers and (iii) a blue nanofiber region on the right. The structural morphology of the electrospun scaffolds is shown in Fig. B, which confirmed nanofiber formation. We will use this new fabrication method to make scaffold libraries where the chemical composition of the nanofibers is varied (not just dye color). We will culture cells on the compositional libraries and characterize their response to demonstrate that the libraries can be used to identify optimal nanofiber scaffold compositions for supporting cell responses such as adhesion, proliferation and differentiation.

In summary, we have developed a new electrospinning technique that is capable of producing nanofiber scaffold libraries containing gradients in nanofiber composition. The gradient nanofiber scaffold libraries will be utilized in screening for nanofiber scaffold compositions that optimize tissue regeneration.

Figures: Gradient nanofiber scaffold library fabrication (A) and structure (B)

left: Dr. Carl G. Simon and right: Dr. Murugan Ramalingam, NRC Associate, NIH (Nibib)/NIST, team members, with their gradient scaffold

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