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Hierarchical design of tunable biomaterial scaffolds for tissue engineering applications

ABSTRACT: Each year millions of Americans receive grafts to replace and repair damaged tissue such as arteries or skin. Autografts are the current gold standard for treatment, however, their limited availability has driven synthetic grafts to become a common alternative. Tissue engineering aims to combine the availability of synthetic grafts with the healing properties of autografts by developing biodegradable synthetic scaffolds that temporarily replace the function of the damaged tissue while promoting and directing neotissue formation. To achieve functional repair, these grafts need to have appropriate mechanical and material properties to restore tissue function, and possess the necessary bioactivity to support cell growth and direct stem cell differentiation throughout remodeling. Electrospinning, a technique to fabricate fibrous scaffolds, has the potential to provide the high degree of control that is needed to meet the requirements of targeted tissue regeneration through modulation of fiber composition, morphology, and macro-architecture. To this end, my work combines biomaterial synthesis and design with the development of new electrospinning strategies to better mimic native tissue structure.

In this work, we detail novel methods to rationally design electrospun tissue engineering scaffolds with defined chemistry and architecture such that degradation rate, bioactivity, release kinetics, and gradient compositions can be tuned to suit the criteria of various applications. In all, these studies aim to advance biomaterial electrospun scaffolds through improved hierarchical design. First, we developed a reactive electrospinning method to crosslink gelatin in situ in order to maintain fiber morphology, and thus scaffold properties, upon implantation with controlled degradation rates. This gelatin platform was then utilized to develop a bilayer wrap with tunable bioactivity to spatially control cellular attachment and prevent intestinal adhesion formation in vivo. Next, the in situ reactive crosslinking methodology, along with a developed in situ photocrosslinking system, were used as tools to tune the release rate of growth factors from electrospun gelatin fibers. Through co-electrospinning these in situ crosslinking strategies, we developed a method to enable independent control over

multi-factor release from a single electrospun mesh. Finally, a novel series of tunable biodegradable polyurethanes were synthesized for interfacial tissue engineering applications. In combination with a new electrospinning method to produce gradients along the direction of fiber alignment, this permitted the formation of parallel mechanical, biochemical, and topographical gradients to better mimic native tissue transitions by spatially controlling cellular behavior.

Overall, this work enhances the capabilities of electrospinning such that we can generate higher functioning grafts with tunable complexities. In addition to providing improved scaffolds for tissue repair, these innovative biomaterials and fabrication strategies provide new tools to probe the complex process of tissue remodeling in order to enhance the rational design of biomaterial scaffolds and guide tissue regeneration strategies. The methods developed here provide a platform for future innovation within biomaterial scaffolds with the potential to fabricate targeted grafts for various applications through rational design.

BIOGRAPHY: Alysha Kishan earned her PhD in biomedical engineering from Texas A&M University in December of last year (2017) under the mentorship of Professor Elizabeth Cosgriff-Hernandez. She completed her in B.S. in biomedical engineering from Duke University in 2011. Her graduate work was focused on the development and synthesis of biomaterial scaffolds for tissue engineering applications. Prior to entering graduate school, Alysha taught high school physics through Teach for America and her passion lies in teaching at all levels. Alysha has given over 7 talks at national/international conferences and has continued to extend STEM curriculum to low socio-economic communities throughout graduate school.