Department of Materials Science and Engineering,

PhD Defense

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Curtis 352

Novel Biomimetic Proteoglycans for Molecular Engineering of the Urethra for Treatment of Stress Urinary Incontinence

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Abstract

Stress urinary incontinence (SUI), which affects approximately 56% of postmenopausal women, is the involuntary leakage of urine through urethra during physical activity. SUI is associated with a decrease in compliance and volume of urethral tissue, which is likely linked to a reduced proteoglycan:collagen ratio in the extracellular matrix (ECM). This thesis work examines the molecularly engineering of the urethra by injecting a novel family of biomimetic proteoglycans (BPGs) into the urethra ex vivo and in vivo. BPGs mimic the 3-D bottlebrush architecture and hydrating properties of natural proteoglycans, and are composed of a synthetic polyacrylic acid (PAA) core (10 kDa or 250 kDa) and natural chondroitin sulfate (CS) bristles (22 kDa). Here, we further characterized BPGs to understand molecular size using dynamic light scattering. Using BPGs, we envisioned modulating physical behavior of the urethra. We hypothesize that through restoration of charge density by introduction of the proteoglycan mimics to the urethral tissue, there will be increased hydration and corresponding improved compliance of the tissue. Here, we examined ex vivo mechanical and physical behavior of porcine urethra in addition to in vivo feasibility of injection of BPGs to the urethra as well as

histological and retention assessment. We put forth that the hydrating properties of BPGs have the ability to increase the volume and improve the compliance of urethral tissue, and thus may have the potential to reverse deteriorative tissue changes and restore urethral tissue to a healthier state. Our findings showed that BPGs were well tolerated in vivo, were retained in the tissue for six weeks, the longest time point examined, and modulated mechanical behavior ex vivo. This work has examined feasibility and mechanisms associated with molecular engineering of the urethra using biomimetic proteoglycans.