PP-10 Engineering A Highly Elastic Scaffold For Urethral Application

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Background: Penile reconstructive techniques that rely on the apposition of two tissues with vastly differing mechanical properties can decrease return of function and increase the risk of short- and long-term complications in this physiologically dynamic organ. The aims of this study were 1) to compare decellularized matrices to urethral tissue and 2) to engineer a novel biomimetic, biocompatible scaffold that reproduces key mechanical properties of healthy urethral tissue. Methods: Hybrid nanofibrous scaffolds were synthesized by electrospinning two naturally derived polymers in random orientation onto a mat: gelatin methacryloyl (GelMA) and elastin-like peptide (ELP). Scaffolds were characterized using NMR spectroscopy, degradation, swelling, tensile and suture testing, and light and scanning electron microscopy. Comparison tensile testing occurred using 1-ply Cook Biodesign small intestinal submucosa, porcine bladder acellular matrix using two protocols (triton-trypsin or SDS-based), and male (4-5mo) New Zealand White rabbit anterior urethra. Onex104 cells/mL human bladder-derived urothelial, smooth muscle cells, or neonatal fibroblasts (ATCC) were seeded onto 1cm2 candidate scaffolds. Cell viability, adhesion/spreading, cytotoxicity and proliferation were evaluated at day 1 to 7 endpoints. T-tests were used for pairwise comparisons; one-way ANOVA for between-group differences. Results: Urethral tissue exhibits remarkable elasticity, whereas acellular matrices are stiffer and stronger substrates (A). 5% GelMA/5% ELP achieved tensile modulus and ultimate tensile strength in static (B) and cyclic testing (not shown) that did not significantly differ from the anterior urethra. Scaffolds were suturable, with improved performance in suture tensile testing with the addition of ELP (C, E). Excellent cell viability was observed from day 1 to 7 across cell lines and scaffolds. While proliferation and spreading of fibroblasts (G) and SMCs (H) was robust, urothelium (I) demonstrated less scaffold adherence and proliferation than the other cell lines. Conclusion: Highly elastic biomimetic scaffolds can be created that mimic the tensile properties of urethral tissue using GelMA/ELP. Future scaffold modifications are ongoing to target urothelial proliferation, and to further define in vitro and in vivo effects of the proposed biomaterials. In the future, highly elastic scaffolds may provide an alternative tissue source for proximal hypospadias repairs.

Keywords: Tissue Engineering, Urethral reconstruction, Proximal hypospadias