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Michael addition reaction to produce the PLA-GLU and PLA-ASP conjugate[1]. Peptide conjugation was characterized via AFM, FTIR and XPS. Next, hMSCs are seeded on the surface modified NF and cultured in osteogenic media for 28 days. Differentiation of MSCs was evaluated by measuring the alkaline phosphatase activity, alizarin red staining, total calcium content, gene expression levels and immunofluorescence staining of osteogenic markers of collagen type I, osteocalcin and osteopontin. Surface characterization of PLA-GLU and PLA-ASP successfully confirms peptide conjugation on NF and osteogenic differentiation of hMSC on surface modified NF are underway. The outcomes of this study would help to determine the most effective sequence on hMSCs on osteogenic differentiation for further modification of the synthetic scaffolds.

1. Karaman O. *et al*, J Tissue Eng Regen Med, **10**(2): p. E132-46(2016).

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Mechanically Tuned Aligned Nanofibers and GDNF to Improve Nerve Growth Conduits

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Treatments for peripheral nerve injury includes autografts and nerve growth conduits (NGC). This project enhances existing NGCs by incorporating aligned nanofibers (topographical) made from a compliant substrate (mechanical) with growth factor (GF) releasing microspheres (chemical). We hypothesize that these cues along with physical therapy (PT) will result in enhanced function recovery. Polycaprolactone conduits with longitudinally aligned methacrylated hyaluronic acid fibers, with or without microspheres containing glial cell line-derived neurotrophic factor were tested in rat sciatic nerves. The animals were divided into five groups: fibers, fibers + PT, fibers + GF, fibers + GF + PT, and autograft control. All animals received behavior and functional testing prior to surgery and weekly post-surgery for 60 days. Prior to sacrifice the Compound Muscle Action Potentials (CMAP) of the gastrocnemius muscles were measured. Gastrocnemius muscles and sciatic nerves were harvested for histological analysis. All surgical procedures and animal testing was approved by the Wayne State University Institutional Animal Care and Use Committee. Weekly testing showed that fibers with GF enhanced or accelerated functional recovery. By 4 weeks both the GF groups were performing similarly to the autograft in the footfall test. Interestingly, starting at week 5, the fibers + PT group was also near autograft. Von Frey fibers were used to test the sensory perception. This study indicates that GFs combined with aligned fibers can improve functional recovery following peripheral nerve injury and that physical therapy can have a positive effect, though it may not have an additive effect when combined with GFs.

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Development of an Elastic and Adhesive Sealant for Surgical Applications

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Conventional surgical sealants have been used for sealing or repairing defects often suffer from low adhesion strength, insufficient mechanical stability and strength, cytotoxic degradation products, and weak performance in biological environments. Therefore, in this study we aimed to engineer a photocrosslinked and highly biocompatible sealant with tunable mechanical and adhesion properties using tropoelastin, as a genetically modified human protein. We tuned the degree of methacrylation of tropoelastin and prepolymer concentration to optimize the physical properties and adhesion strength of the methacryloyl-substituted tropoelastin (MeTro) hydrogel for sealing of elastic and soft tissues. Following ASTM standard tests, the MeTro hydrogels revealed superior adhesive strength and burst pressure values compared to the commercially available sealants. The subcutaneous implantation of the engineered MeTro hydrogels in rats exhibited minimal inflammatory host responses and slow biodegradation of sealant. The *in vivo* and *ex vivo* burst pressure resistance of bioengineered MeTro sealants was tested on lungs and arteries in small as well as translational large animal models. Our results proved MeTro sealant to effectively seal lung and artery leakages without the need for sutures or staples, presenting a significant improvement compared to the commercially available clinical sealants (Evicel® and Progel™) and sutures only. Combining these results, we envision that the engineered MeTro sealant has the potential to be commercialized due to its remarkable mechanical strength, biocompatibility, biodegradability and strong adhesive interaction between the sealant and the wound tissue without the need for suturing.

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Seeding and Recellularization of Porcine Acellular Muscle Matrix Biomaterials with Adipose-Derived Mesenchymal Stem Cells and C_2C_{12} Myoblasts

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The ability of skeletal muscle to repair itself via regenerative mechanisms is limited to instances where tissue damage is relatively small. When volumetric muscle loss occurs, the regenerative capacity of skeletal muscle is exceeded. This results in a permanent loss of muscle volume and function. Current strategies to replace or repair such damage are inadequate. The goal of this project is to develop natural biomaterials that facilitate the engineering and/or regeneration of skeletal muscle tissue by providing a myoinductive environment to seeded and/or infiltrating cells. We hypothesized that scaffolds and hydrogels composed of porcine acellular muscle matrix (PAMM) could be efficiently recellularized and support myogenic differentiation. Here, we describe the production and characterization of PAMM scaffolds and gels. Histological analyses, DNA content measurement, and scanning electron microscopy show that porcine skeletal muscle tissue can be effectively decellularized and processed into both a sheet-like scaffold and a hydrogel. We also demonstrate that PAMM biomaterials can be recellularized with adipose-derived mesenchymal stem cells and support the differentiation of C_2C_{12} myoblasts into myotubes. These results demonstrate the potential for PAMM biomaterials to be employed in tissue engineering and regenerative medicine-based strategies for repairing volumetric muscle loss.

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Bioprinting of Engineered Heart Tissue

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For cardiac tissue repair, 3D bioprinting holds great potential enabling to create multicellular constructs with defined shape and cell composition. However, materials selection and effective structures that can be reliably used to bioprint cardiac tissue constructs remain elusive. Here we present a concerted effort to fine tune