**DEVELOPMENT OF A COMPOSITE ACELLULAR TISSUE GRAFT FOR MUSCULOSKELETAL TISSUE ENGINEERING**

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## ABSTRACT

A composite acellular tissue graft comprised of decellularized tendon conjugated with nanomaterials has been developed for musculoskeletal tissue engineering applications. The focus of this dissertation is on the development of composite grafts derived from decellularized human tendon conjugated with gold nanoparticles and hydroxyapatite nanoparticles for use in anterior cruciate ligament (ACL) reconstruction. Gold nanoparticles are used to promote remodeling, cellularity, and biological incorporation of grafts. Hydroxyapatite nanoparticles are used to promote osseointegration, cellularity, and to enhance the graft/bone interface. These composite grafts along with several other variations, were characterized *in vitro* using a variety of cell-based assays including cell viability, cell proliferation, and cell migration assays. Two *in vivo* studies were conducted. A green fluorescent protein (GFP) porcine model was investigated as a new method to evaluate host tissue integration into soft tissue grafts as well as the *in vivo* biocompatibility of subcutaneously implanted composite grafts. Results demonstrate biocompatibility and remodeling of composite grafts and the value of using the GFP model as a qualitative method for assessing host tissue integration. A rabbit ACL reconstruction model was used to investigate graft remodeling in addition to the overall viability of using composite grafts to serve as a functional ACL replacement. Results demonstrate successful replacement of ACLs using composite grafts with enhanced remodeling from the addition of nanoparticles. Overall, studies demonstrate the success and potential further application of using composite grafts for musculoskeletal tissue engineering applications. Future studies will include expanding development of variations of these composite materials to address additional clinical needs.