Development of a Biomimetic, Collagen-Based Scaffold for the Repair and Regeneration of the Annulus Fibrosus

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Annually, millions of Americans are diagnosed with intervertebral disc (IVD) disorders: IVD herniation (IVDH- structural disruption of the annulus fibrosus (AF)) and/or degeneration (IVDD- a multifactorial degradation process initiating in the central gelatinous core: nucleus pulposus (NP)). Both disorders result in similarities, such as impaired mechanical function, with current palliative treatments failing to address the remnant structural AF focal defects; thus, leading to re-herniation and/or IVDD progression. To address this, we have developed a 3-layered biomimetic, collagen-based scaffold from decellularized pericardium (AF repair patch (AFRP)), which mimics the native structure, biochemistry, & uniaxial tensile mechanical competency essential for the closure of AF focal defects. The objectives herein were to further characterize the AFRP for its ability to: 1) demonstrate similar native AF structure & mechanical properties, 2) promote cell-mediated tissue regeneration \textit{in vitro}, & 3) demonstrate biocompatibility while promoting tissue regeneration \textit{in vivo}.

First, AFRPs were evaluated for their ability to mimic the AF’s native “angle-ply” architecture, mechanical properties (uniaxial & biaxial tension, attachment strength, & impact resistance), & relative impact on axial/torsional kinematic parameters. Next, AFRPs were crosslinked in 6mM/1.2mM EDC/NHS & assessed for their tissue regenerative capability through cell cytocompatibility, differentiation of mesenchymal stem cells (MSCs), & long-term tissue remodeling. Additionally, independent MSC origins were evaluated for the ability to repair IVD tissues under normal & INF culture conditions. Lastly, an ovine model of IVDD was developed & characterized to assess the AFRPs ability to support IVD repair & its potential to regenerate the damaged tissue following implantation into a degenerated IVD (in conjunction with a preformed NP biomaterial).

Overall, AFRPs demonstrated compelling similarities to the native AF. The AFRPs inherent collagen fibers mimicked the native AF’s “angle-ply” architecture, which played a significant role in the AFRPs ability to mimic physiological mechanical properties required for natural AF movements: flexion, extension, rotation, & high impact activities. Moreover, adipose-derived MSC-seeded AFRPs microarchitecture & biochemical cues promoted tissue regeneration through the differentiation of MSCs towards an AF cell phenotype in the absence of media supplementation & mechanical stimulus; however, this was detrimentally affected by inflammation (INF). Although, amnion-derived MSCs highlighted positive chondroprotective properties needed for IVD repair compared to adipose-derived MSCs in both normal and INF cultures. Moreover, long-term culture of these AFRPs demonstrated tissue remodeling as observed with changes in biaxial mechanics & deposition of new immature collagen. Furthermore, degenerate ovine IVDs repaired with AFRPs \textit{in vivo} demonstrated the ability to support AF tissue repair & regeneration through the restoration of imaging modalities & mechanical parameters in addition to preventing NP herniation.

Collectively, results herein suggest the AFRPs potential to serve as an AF repair biomaterial to augment the current IVDH and IVDD surgical procedures to permit improved patient outcomes through fewer revision surgeries via lower re-herniation & expulsion rates, respectively.

\textbf{November 26th, 2018 (6:00 PM)}

\textbf{Rhodes Annex 111, Clemson University, Clemson, SC}