Characterizing Discogenic Cell Based Tissue Engineered Disc Replacements

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INTRODUCTION: Current treatments for back pain associated with late-stage intervertebral disc (IVD) degeneration may temporarily relieve pain through fusion. However, they do not restore biological and mechanical function to the disc. The use of living tissue engineered constructs to replace degenerated discs has the potential to overcome these limitations and has been investigated in vitro by a number of groups.1 Our group developed endplate-modified disc-like plex structures (eDAPS) that mimics the native structure and function of the disc.2

RESULTS: The ratio of gene expression for ACAN / COL1A2 related to mesenchymal and intervertebral IA2. (C) Cell surface expression of markers for ACAN / COL1A2. (D) HPRT1 gene expression for ACAN / COL1A2. (Figure 1A). Measurement of secreted proteins showed that NP cells grown in suspension culture had a greater aggrecan / collagen 1 ratio than either AF or NP cells grown in attachment culture (Figure 1B). All cell surface markers tested showed similar expression between the AF and NP cells (Figure 1C). eDAPS cultured with attachment- or suspension-derived Discogenic NP cells were histologically, mechanically, and biochemically similar. Att. or Susp. NP cells deposited more proteoglycans in the NP region of the eDAPS than the goat MSCs (Figure 2A). Discogenic eDAPS were mechanistically distinct from MSC eDAPS and had increased toe modulus (Figure 2B), increased linear modulus (Figure 2C), and decreased compressive stress to goat MSC eDAPS (Figure 2D). Both Discogenic eDAPS were mechanically similar, and both Discogenic NP cells produced the same amount of GAG (Figure 2E) and collagen (Figure 2F). Discogenic AF cells produced a minimal amount of GAG.

DISCUSSION: Characterization of Discogenic Cells prior to seeding indicated that all cells embodied a progenitor phenotype, expressing extremely low levels of CD24. Discogenic NP cells cultured in suspension initially produced greater amounts of aggrecan than NP cells cultured via attachment, but eDAPS cultured with both cell types were similar in every outcome measured. It is likely that both cell populations performed similarly once transitioned to 3D culture as NP cells expanded in monolayer have been shown to develop normal NP phenotypes following 3D culture.4 Unfavorable diffusion gradients often create hostile environments for cells toward the center of large implants that result in heterogeneous matrix deposition,2 as was observed in MSC-seeded eDAPS. Critically, the deposition of proteoglycans in the NP was more homogeneous in eDAPS seeded with Discogenic NP cells, indicating that Discogenic Cells more readily thrived in the unfavorable environment of a human-sized disc. Additionally, the NP and AF regions of Discogenic eDAPS were biochemically distinct, whereas goat MSC eDAPS regions were less defined with increased collagen deposited along the outer edges of the NP. Future work will involve the creation of human Discogenic eDAPS as well as in vivo evaluation of Discogenic eDAPS in our established large animal model.

SIGNIFICANCE: Discogenic Cells are a promising development in the translation of tissue engineered therapies that remove the many hurdles of working with native human disc cells. Discogenic Cells were shown to be safe in clinical trials for patients with mild to moderate lumbar disc degeneration and produced clinically meaningful improvements in low back pain, function and quality of life. This work further advances translation by culturing tissue engineered discs at a scale appropriate for human cervical disc replacement using a translatable human NP and AF cell source.


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