Assessing the Regenerative Capacity of Amniotic Stem Cell Seeded Nucleus Pulposus and Annulus Fibrosus Implants in an Injured and Inflamed Intervertebral Disc Explant Organ Culture
Jeremy J. Mercuri, PhD; Sanjitpal S. Gill, MD

Purpose
Intervertebral disc (IVD) degeneration (IVDD) is a cell-mediated, inflammatory process that initiates the proteolytic destruction of the nucleus pulposus (NP) and can lead to focal rupture of the annulus fibrosus (AF). As a consequence, normal spine function is impaired resulting in altered kinematics, low back pain, long-term disability and significant socioeconomic burden. Patients with IVDD could benefit from early-stage treatments including NP replacement and repair of damaged AF tissue with biomimetic implants that can immediately restore IVD function while promoting the long-term regeneration of the two tissues. Our research group has created two innovative extracellular matrix (ECM)-based implants which mimic the native biochemistry, structure and mechanical properties of NP and AF tissue, respectively. These implants also support amniotic mesenchymal stem cell (AM-MSC) viability; a regenerative cell source which may have the potential to promote IVD tissue regeneration in the presence of inflammation. Thus, the purpose of the proposed work is to determine the therapeutic potential of our implants, in conjunction with hAMSCs, to support NP and AF tissue repair and regeneration in an injured and inflamed IVD organ culture model.

Hypothesis
Human AM-MSC-seeded NP and AF repair implants will rescue injured and inflamed IVDs by promoting in situ tissue regeneration, implant integration, and restoration of IVD function and microarchitecture towards uninjured levels.

Method of Research
An ex vivo bovine IVD organ culture model and bioreactor system will be utilized to test the hypothesis. Briefly, bovine tail IVD (btIVD) explants will be injured via annulotomy and sub-total nucleotomy prior to repair with hAMSC-seeded NPR and AFRP implants. Repaired btIVDs will be maintained in inflammatory culture reminiscent of degenerate human lumbar IVDs under diurnal compressive loading using a simple, scalable bioreactor for up to 30 days. Regeneration will be assessed via compressive kinematic testing, biochemical assays and histological assessments. Unrepaired btIVDs and those repaired with non-cell-seeded implants will serve as comparative controls.

Expected Results
Repair of btIVDs with hAMSC-seeded NP and AF implants will result in tissue regeneration as evidenced by deposition of new glycosaminoglycan (GAG) and collagen, extracellular matrix micro-architectural remodeling and improved axial kinematic parameters compared to controls.