Orthopaedic Surgery
School of Medicine
University of Missouri Health

Metabolic Responses of Degenerative Intervertebral Discs from Patients Undergoing Cervical or Lumbar Spinal Fusions

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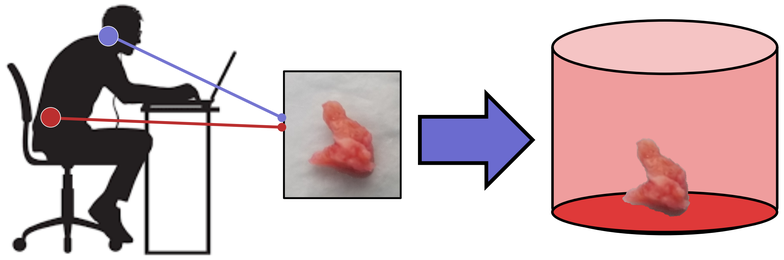
Introduction and Purpose

- Intervertebral disc (IVD) degeneration encompasses a spectrum of disorders that involve maladaptive biomechanical and cellular responses to chronic loading, insult, and injury that vary based on a number of factors including anatomic location
- It is not known if mechanism of IVD degeneration are significantly different between the cervical and lumbar spine
- This study aims to characterize relevant biomarker profiles for degenerative cervical and lumbar IVDs

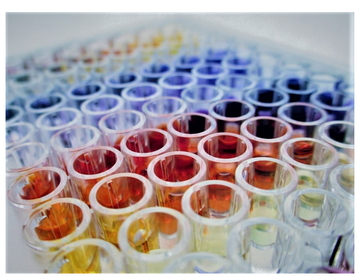
Hypothesis

Degenerative lumbar IVD tissues will produce significantly higher levels of inflammatory and degradative biomarkers by compared to degenerative cervical IVD tissues with or without cytokine stimulation

Methods



1) With IRB approval, cervical and lumbar IVD tissues otherwise discarded after surgery were collected from patients (n=145, mean age 57y, 92F) being surgically treated for symptomatic degenerative IVD disorders
2) IVD tissue explants (n=2/patient/disc segment) were created using a 6 mm diameter biopsy punch and cultured for 3 days with and without 10 ng/ml IL-1β stimulation. Media were collected on day 3 of culture for biomarker analyses



3) Media were tested for MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-13, TIMP-1, TIMP-2, TIMP-3, TIMP-4, GRO-α, MCP-1, MCP-3, PDGF-AA, PDGF-AB/BB, IL-1, IL-4, IL-6, IL-8, MIP-α, MIP-β, RANTES, TNF-α, and VEGF using Luminex xMAP assays according to the manufacturer's protocol
4) The media biomarker concentrations were standardized to tissue wet weight for statistical analysis. Linear mixed models were used and log transformations were performed. Statistically significant differences were determined with adjustment for BMI group and Age group with α = 0.05.

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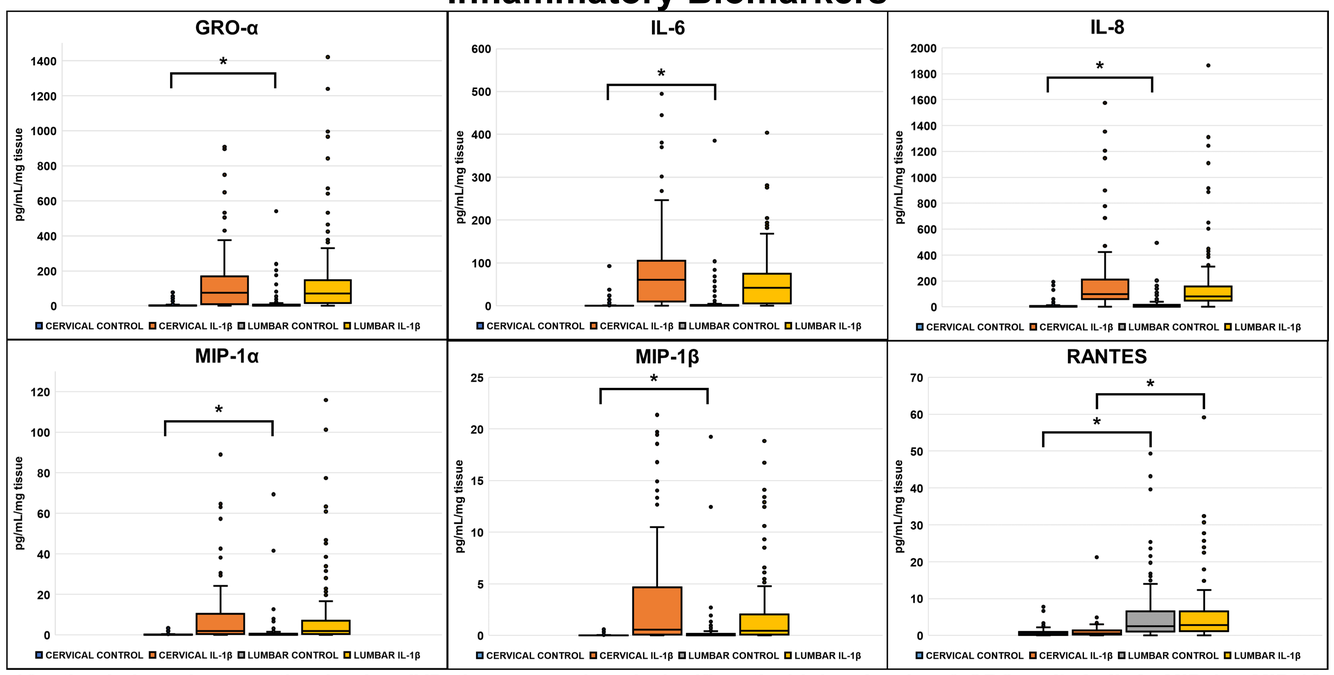
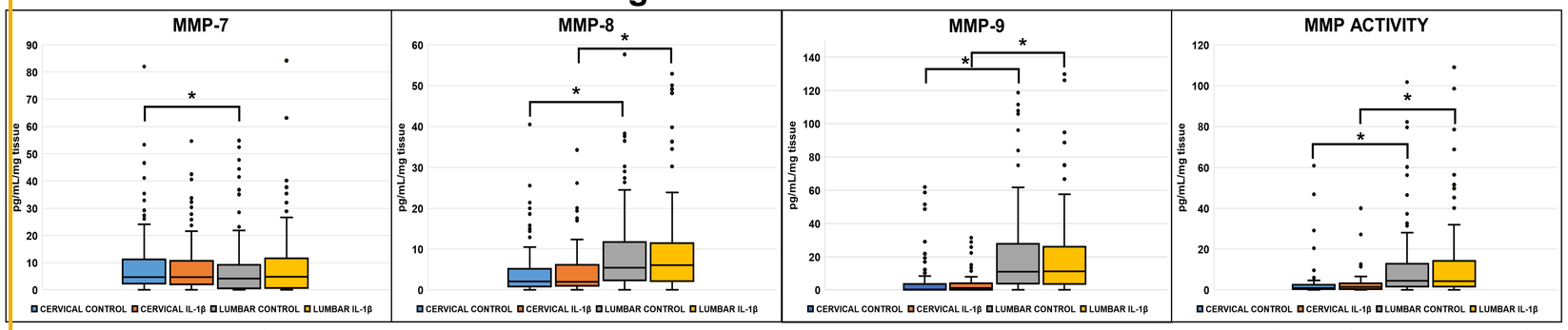
Results and Discussion

Inflammatory Biomarkers



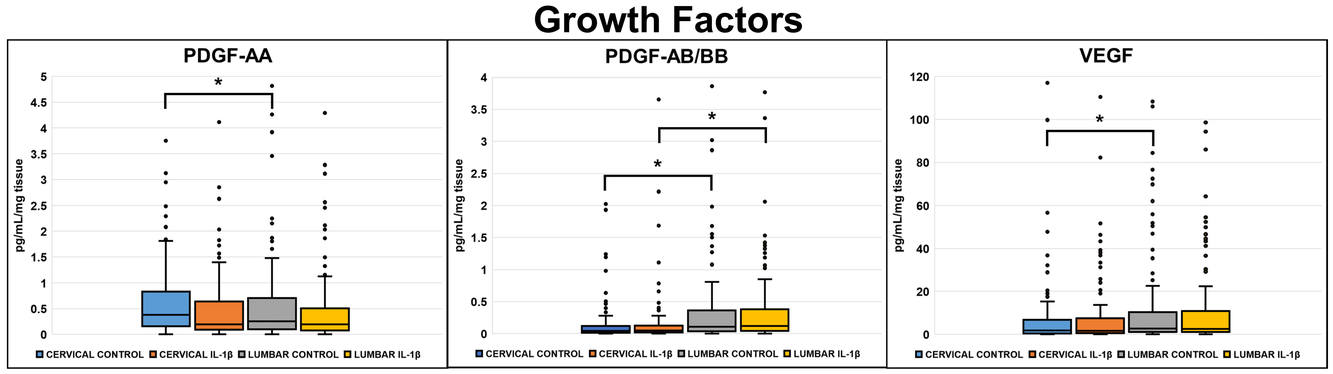
- Without IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of GRO-α, IL-6, IL-8, MIP-1α, MIP-1β, and RANTES compared to degenerative cervical IVD tissues.
- With IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of RANTES compared to degenerative cervical IVD tissues

Degradative Biomarkers



- Without IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of MMP-8, MMP-9, and MMP activity, and lower MMP-7, compared to degenerative cervical IVD tissues
- With IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of MMP activity, MMP-8, and MMP-9 compared to degenerative cervical IVD tissues

Growth Factors



- Without IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of PDGF-AB/BB, VEGF, and significantly lower levels of PDGF-AA, compared to degenerative cervical IVD tissues.
- With IL-1β stimulation, degenerative lumbar IVD tissues produced significantly higher levels of PDGF-AB/BB compared to degenerative cervical IVD tissues.

Conclusions

- This data expands on previous studies findings indicating degenerative lumbar IVDs have a more pro-inflammatory and pro-degradative basal metabolism compared to degenerative cervical IVDs.
- Degenerative cervical and lumbar IVDs showed similar metabolic responses to pro-inflammatory cytokine stimulation.
- Determining how these differences in tissue metabolism relate to clinical disease may allow for the development of novel, site-specific diagnostic and treatment strategies for IVD degeneration