Lumbar intervertebral disc mRNA sequencing identifies the regulatory pathway in patients with disc herniation and spondylolisthesis

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Disclosures

Nothing to disclose
Introduction

- Lumbar degenerative disc disease (DDD) is a multifaceted progressive condition
- DDD may lead to spinal stenosis, disc herniation (DH), and/or degenerative spondylolisthesis (DS)
- Here, we evaluated transcriptome profiles of a cohort of 10 human lumbar disc tissue with musculoskeletal tissues.

A. Disc herniation (DH)  B. Degenerative spondylolisthesis (DS)
Results -
Characteristics of all groups:

Characteristics of patients with lumbar NP:

<table>
<thead>
<tr>
<th>Samples</th>
<th>Age (Year)</th>
<th>Sex</th>
<th>BMI</th>
<th>Level</th>
<th>Pre-operative Diagnosis</th>
<th>Modified Pfirrmann disc degeneration grade</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>M</td>
<td>23.6</td>
<td>L5-S1</td>
<td>DH</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>M</td>
<td>32</td>
<td>L4-L5</td>
<td>DH</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>F</td>
<td>27.7</td>
<td>L5-S1</td>
<td>DH</td>
<td>6</td>
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<tr>
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<td>M</td>
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<td>L5-S1</td>
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</tr>
<tr>
<td>6</td>
<td>63</td>
<td>M</td>
<td>28.6</td>
<td>L5-S1</td>
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<tr>
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<td>L5-S1</td>
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<td>6</td>
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<td>8</td>
<td>41</td>
<td>M</td>
<td>27.5</td>
<td>L5-S1</td>
<td>DS</td>
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<tr>
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<td>M</td>
<td>27.35</td>
<td>L5-S1</td>
<td>DS</td>
<td>8</td>
</tr>
</tbody>
</table>
Comparative analysis of mRNA expression in lumbar NP vs musculoskeletal tissues:

A. PCA plot showing gene expression across different tissue types. 

B. Hierarchical clustering of gene expression data across lumbar NP, Bone, Growth Plate, Cartilage, and Muscle.

C. Categories: Lumbar NP, Bone, Growth Plate, Cartilage, Muscle.

D. Volcano plot illustrating significant gene expression differences.

E. Bar chart showing enrichment analysis of biological processes.
Comparative analysis of mRNA expression in between DH and DS:

A. Comparative analysis of mRNA expression in between DH and DS:

B. Venn diagram showing the number of genes specific to each condition:
   - Disc Herniation: 736 (4.9%)
   - Degenerative Spondylolisthesis: 811 (5.4%)
   - Overlap: 13355 (89.6%)

C. Bar chart showing the expression levels of different proteins:
   - Thrombospondin
   - Lipoprotein
   - IGF binding protein

D. Bar chart showing the expression levels of different functional categories:
   - Signal
   - Acetylation
   - Immunity
   - Immunoglobulin-like fold
Signaling networks identified within the DH and DS:

A. [Diagram showing Signaling networks]

B. [Diagram showing Signaling networks]

C. [Graph showing MMP16 expression]

D. [Graph showing ADAMTS1 expression]

E. [Graph showing ADAMTS5 expression]

F. [Graph showing ADAMTS8 expression]

G. [Graph showing CDH1 expression]

H. [Graph showing EPHA1 expression]

I. [Graph showing EFNA2 expression]
Discussion

• We have identified gene regulatory networks in DH and DS tissues that are associated with regulation of extracellular matrix synthesis and inflammatory response.

• Results from these studies can be used to optimize and validate tissue engineering strategies and develop novel pharmacologic approaches for the treatment of Lumbar DDD.
Summary Points

• We identified differentially expressed mRNAs in degenerated lumbar disc compared to musculoskeletal tissues.

• Disc herniation and spondylolisthesis result in disease related gene expression.

• Degeneration disc disease activates multiple molecular pathways.