



Human Cell Transcriptomic Differences Between Hypertrophic and Normal Ligamentum Flavum in Chronic Lower Back Pain

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BACKGROUND

- Lumbar spinal stenosis (LSS) is the most common cause of spinal surgery¹ and affects 50% of individuals aged 70 years or older.²
- Hypertrophied ligamentum flavum (HLF), is known to be the key contributor to development of LSS.³
- Chronic lower back pain (CLBP) has a lifetime prevalence of 80% amongst adults⁴ and is also significantly associated with HLF.⁵
- HLF is also associated with decreased elastic fibers and increased proteoglycans and collagen, but little else is known regarding the cellular landscape and intracellular level differences between HLF and normal ligamentum flavum (NLF).⁶

STUDY AIMS

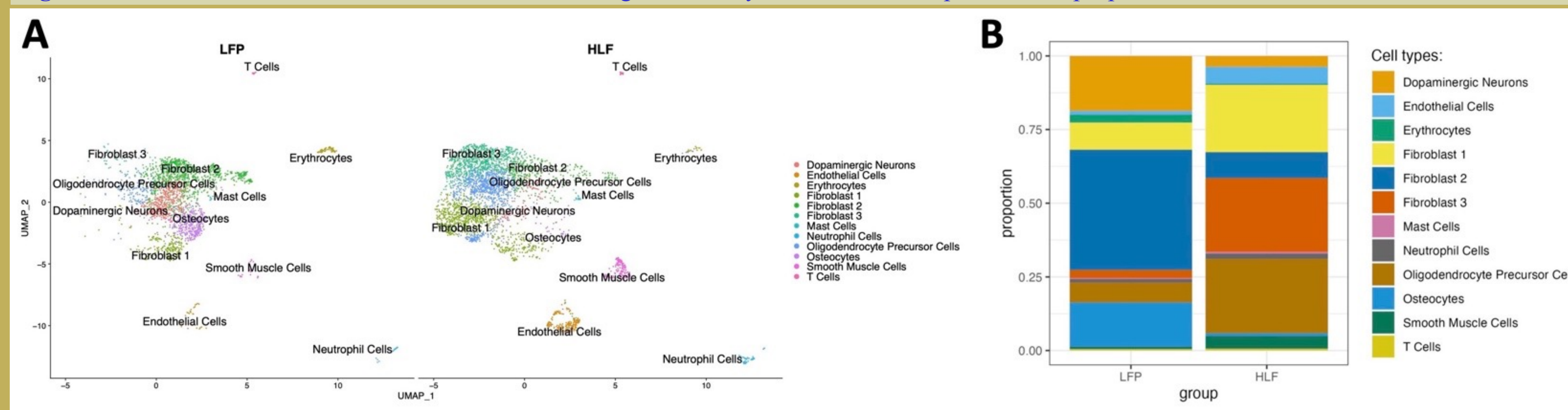
The aim of the study is to investigate single cell transcriptomic differences between HLF and NLF in patients with CLBP.

METHODS

- Highly advanced 10X Genomics Chromium single cell RNA Sequencing was performed on one human NLF and one human HLF from a patient with CLBP undergoing lumbar spine surgery.
- Cells were clustered and annotated with ScType using publicly available cell type and annotation markers.
- A custom algorithm (Nested Hierarchical Dirichlet Processes) for a non-parametric statistical model was used to discover gene expression modules (GEMs) that are repeatedly co-expressed in many cells.

RESULTS

Figure 1. Panel A: Annotated cluster of LFP and HLF single cell analysis; **Panel B:** Bar plots of cell proportions.



DISCUSSION

- Study offers novel characterization of HLF at large
- HLF and NLF have differential single cell landscapes and GEMs
- Specifically, the composition varies greatly by subtype of fibroblasts (Type 1, 2, and 3)
- Novel intracellular differences found demonstrate the feasibility of doing single cell transcriptomics to uncover additional cellular differences between HLF and NLF
- Further studies have the potential to reveal modulators – including the roles of neuronal and immune cells – in CLBP and surgical pain, as well as insight into targeted inhibition of specific cellular hypertrophy to prevent CLBP

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ADDITIONAL INFORMATION

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- Both contain a mixture of cell types including neuronal, endothelial and immune cells
- Predominantly composed of fibroblasts cells
- The fibroblast composition of the two samples are different
- NLF had a greater number of fibroblast type 2
- HLF had more fibroblast types 1 and 3
- Expression of genes such as *MMP1* (which is involved in extracellular matrix remodeling) and some collagen genes such as *COL1A1* appear to be fibroblast subtype specific
- Several highly significant GEMs were found for ECM, collagen degradation, laminin interactions and cholesterol biosynthesis in specific subsets of cells (data not shown)

Figure 2. Feature plots of *MMP1* and *COL1A1*.

