Hypertrophy of the Ligament Flavum in Degenerative Lumbar Stenosis Associated with the Increased Expression of Fractalkine (CX3CL1)/CX3CR1 Chemokine

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Introduction

1. Fractalkine (CX3CL1)

1) adhesive and migratory functions by interacting with the chemokine receptor CX3CR1

2) Fractalkine (CX3CL1) and its receptor (CX3CR1) comprise a chemokine system involved in leukocyte recruitment and adhesion in chronic inflammatory disease
To investigate

1) The role of CX3CL1/CX3CR1 chemokine on hypertrophy of the ligament flavum (LF) in degenerative lumbar stenosis (DLS) compared with that of non-degenerative spinal condition (NDS) of the lumbar spine.

2) Correlation between expression of CX3CL1/CX3CR1 chemokine and thickness of LF.
1. 21 patients were enrolled in this study. 
   10 patients were diagnosed with spinal stenosis
   11 others with non-stenotic spinal disease (NDS)

2. Decompressive surgery was performed
   LF was harvested from L4–L5 in each patient.

3. Mean (SD) age: 72.1 (7.7) years in the LSS group
   59.6 (16.6) years in the control group.
Material & Method


2. The mRNA concentrations of CX3CL1/CX3CR1 chemokine: real-time PCR

3. Localization of CX3CL1/CX3CR1 chemokine: immunohistochemical study

4. Plasma levels of soluble FKN, ELISA
The mean thickness of the LF
4.68 ± 1.54 mm from SS group
3.05 ± 1.47 mm from NDS group.

The difference was significant (P = 0.006)
Results

CX3CL1 Expression by Immunohistochemical Analysis

A
B
C
D
Results

CX3CR1 Expression by Immunohistochemical Analysis

A

B

C

D
## Results

**CX3CL1/CX3CR1 mRNA Expression by RT-PCR**

<table>
<thead>
<tr>
<th>Variables</th>
<th>DLS $\pm$ SEM</th>
<th>NDS $\pm$ SEM</th>
<th>P-value $^a$</th>
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<tr>
<td>Positive cell ratio by Immunohistochemistry</td>
<td>CX3CL1 $^c$</td>
<td>43.70 $\pm$ 20.42</td>
<td>27.10 $\pm$ 9.689</td>
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<td>CX3CR1 $^c$</td>
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<td>Relative amount of mRNA by quantitative real-time PCR</td>
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$^a$Statistical significance test was done by Mann-Whitney U test. $^c$

*P* value $< 0.05$ was significant and shown in bold. $^c$
## Results

Serum levels of soluble CX3CL1

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Results

Correlation of serum CX3CL1 level, mRNA Expression of CX3CL1/CX3CR1 and the thickness of LF

(A) FKN mRNA expression (FKN/GAPDH) vs. Thickness of LF (mm)

Y = 0.532X + 2.612

R² = 0.671, P < 0.05

(B) CX3CR1 mRNA expression (CX3CR1/GAPDH) vs. Thickness of LF (mm)

Y = 3.551X + 2.525

R² = 0.514, P < 0.05

(C) FNK (ng/mL) vs. Thickness of LF (mm)

Y = 1.046X + 3.257

R² = 0.197, P < 0.05

(D) Age (year) vs. Thickness of LF (mm)

Y = 0.044X + 0.966

R² = 0.137, P = 0.099
Conclusion

- The activity of fractalkine and CX3CR1 was established in ligament flavum by immunohistochemistry, ELISA, and quantitative real-time PCR.

- There was a significantly increased expression of the fractalkine and CX3CR1 in ligament flavum in degenerative lumbar stenosis compared with non-degenerative spinal condition.

- Increased fractalkine and CX3CR1 activity in the ligament flavum in patients with degenerative lumbar stenosis may represent one of the pathologic mechanisms of the hypertrophied ligament flavum.
Declaration of interest

The authors report no conflicts of interest.