Previously, we reported that interleukin-18 (IL-18) may promote stromal hyperplasia in the prostate by inducing production of thrombospondin-1 (TSP-1) using cultured cells. (Hamakawa et al. Prostate. 2014)

In this study, we aimed to determine the expression levels of IL-18 and TSP-1 in human prostate tissue and assess the roles of these expressions as biomarkers to diagnose the progression of BPH.

**Hypothesis / aim of study**

**Study design, materials and methods**

**Study 1**

- **Subject**
  16 patients without malignancy who underwent transperineal prostate biopsy and measured the prostate volume by transrectal ultra-sonography at our institution. Prostate tissues were obtained from the transitional zone.

- **The evaluation of mRNA expression**
  The expression levels of mRNAs in these tissues were evaluated by quantitative real-time reverse transcription polymerase chain reaction (qPCR).
  mRNAs; IL-18, IL-18 receptor, TSP-1

- **Statistical analysis**
  The correlation between mRNA expression levels and variables were evaluated by Pearson’s product-moment correlation coefficient.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>66.1 ± 12.5</td>
</tr>
<tr>
<td>TPV (ml)</td>
<td>35.5 ± 20.1</td>
</tr>
<tr>
<td>TZV (ml)</td>
<td>17.4 ± 14.1</td>
</tr>
<tr>
<td>T2I</td>
<td>0.43 ± 0.16</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>6.71 ± 3.96</td>
</tr>
</tbody>
</table>

Pearson's correlation coefficients

- IL-18
  - Age: -0.164
  - TPV: -0.244
  - TZV: -0.18
  
- IL-18R
  - Age: -0.013
  - TPV: -0.065
  - TZV: -0.128
  
- TSP-1
  - Age: 0.473
  - TPV: 0.729
  - TZV: 0.884
  
- PSA (ng/ml)
  - Age: 0.211

TSP-1 expression was positively correlated with TPV and TZV.

**Study 2**

- **Subject**
  Samples from 8 of the patients in Study 1

- **The correlation between mRNA expression and the change in TPV**
  The volume of the prostate was measured at biopsy and at a given point in time after biopsy. The correlation between the increment in TPV per day and mRNA expression evaluated by Pearson’s product-moment correlation coefficient.

- **Patient characteristics**
  Prostate biopsy and any given point in time

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>67.9 ± 7.6</td>
</tr>
<tr>
<td>TPV (ml)</td>
<td>40.5 ± 19.0</td>
</tr>
<tr>
<td>TZV (ml)</td>
<td>20.4 ± 13.2</td>
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<tr>
<td>T2I</td>
<td>0.45 ± 0.17</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>9.23 ± 3.31</td>
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<tr>
<td>observation period (day)</td>
<td>835.1 ± 412.2</td>
</tr>
<tr>
<td>increase in TPV (ml)</td>
<td>12.4 ± 12.5</td>
</tr>
<tr>
<td>increase in TPV per day (ml/day)</td>
<td>0.0703 ± 0.0014</td>
</tr>
</tbody>
</table>

Pearson's correlation coefficients

- IL-18
  - Increase in TPV per day: 0.178
  - Increase in TPV: 0.189
  - TSP-1: 0.717

There was a strong positive correlation between the increment in TPV per day and TSP-1 expression.

**Interpretation of results**

TSP-1 is an extracellular matrix and has shown to be a regulator of angiogenesis and an activator of latent transforming growth factor beta (TGF-b).

Previously, we reported that TSP-1 promoted the proliferation of prostatic stromal cells and it might induce the development of prostatic stromal hyperplasia.

Thus, we consider that the higher expression of TSP-1 may reflect large prostate size and the increment in prostate volume. It may contribute the progression of benign prostatic enlargement.

**Concluding message**

- TSP-1 was positively correlated with prostate volume and the increase in prostate volume per day.
- This result suggested that TSP-1 might have a potential biomarker predicting the progression of BPH.

The authors declare no conflict of interest associated with this presentation.