INTRODUCTION

• The involvement of mast cells in interstitial cystitis (IC) has been indicated.
• Kynurenine, one of the tryptophan metabolites, is an endogenous agonist of aryl hydrocarbon receptor (AhR).
• Kynurenine/AhR signaling has been reported to regulate mast cell activation.

We examined the role of kynurenine/AhR signaling in the pathology of IC using a rat model of cyclophosphamide (CYP)-induced cystitis.

METHODS

◆ Animals
10- to 11-week-old female Wistar/ST rats

◆ Protocol

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Evaluation</th>
<th>Control+vehicle</th>
<th>Control+MT</th>
<th>CYP+vehicle</th>
<th>CYP+MT</th>
</tr>
</thead>
<tbody>
<tr>
<td>saline, i.p.</td>
<td>bladder function (cystometry)</td>
<td>△</td>
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<tr>
<td>saline, i.p.</td>
<td>mRNA expression levels (real-time PCR)</td>
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<tr>
<td>CYP 150 mg/kg, i.p.</td>
<td>kynurenine content (UPLC-MS/MS)</td>
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MT : 1-methyl-L-tryptophan (an inhibitor of IDO1)
△ : vehicle (1% HPMC) △ : MT (100 mg/kg/day)

RESULTS

◆ Cystometry

<table>
<thead>
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<tr>
<td>Intercontraction intervals</td>
<td>△</td>
<td>△</td>
<td>△</td>
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<td>Maximum pressure</td>
<td>△</td>
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The inhibition of the kynurenine pathway improved the intercontraction intervals of CYP-induced cystitis rats.

◆ The kynurenine content in the bladders

The kynurenine content in the cystitis rats was higher than that of control rats and suppressed by MT.

◆ The mRNA expression levels in the bladders

In the bladders of the CYP-induced cystitis models, kynurenine/AhR signaling was enhanced and suppressed by MT.

CONCLUSIONS

• The kynurenine/AhR signaling was enhanced in the bladders of cystitis rats and suppressed by MT.
• Inhibition of the kynurenine synthesis improved the urinary symptoms.

Our study suggests that the kynurenine/AhR signaling might be a new target for treatment and prevention of IC.

DISCLOSURE

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