

INCREASED MRNA EXPRESSION OF CONNEXINS AND TRANSIENT RECEPTOR POTENTIAL CHANNELS IN THE UROTHELIUM OF PATIENTS WITH INTERSTITIAL CYSTITIS: POSSIBLE BIOMARKERS

Hypothesis / aims of study

Interstitial cystitis (IC) is a disease characterized by bothersome lower urinary tract symptoms including bladder hypersensitivity, urinary frequency and bladder pain, which severely impair patient's quality of life. However, pathophysiology of IC remains unclear despite the struggle for the development of new biomarkers to diagnose IC and effective therapeutic interventions. In the present study, to explore pathophysiology of IC, we investigated mRNA expression of connexions (Cx) and transient receptor potential (TRP) channels in the urothelium.

Study design, materials and methods

Eleven patients with IC for hydrodistension or 17 patients with no invasive bladder cancer who underwent transurethral resection as normal controls (NL) were enrolled in the present study. Under cystoscopy, bladder specimens were obtained before hydrodistension or tumor resection with cold cup biopsy forceps. In IC patients with ulcerative lesion, bladder specimens were obtained from the ulcerative region. Apparently normal tissue in patients with bladder cancer was used as NL. Total RNA was extracted from bladder samples and RT-PCR was performed according the manufacturer protocol. Each experiment was performed 3 times and average values normalized to β -actin were used for analysis.

Data were presented as a group mean \pm standard deviation. Statistical analyses were performed using Mann-Whitney U test and $p < 0.05$ was considered statistically significant.

Results

Cxs-mRNA, including Cx26, Cx32, Cx40 and Cx43, were analyzed using RT-PCR. Results of RT-PCR were shown in Figure 1. All mRNA expression of these Cxs was significantly increased in the urothelium of IC patients. Regarding TRP-mRNA, we analysed TRPV1, TRPV2, TRPM2 and TRPM7. As shown Figure 2, only TRPM2-mRNA was significantly increased in the urothelium of IC. TRPV2-mRNA showed a trend of increased expression. However, there was no significant difference in the other TRPs-mRNA expression between IC and NL. In addition to Cxs and TRPs, NGF-mRNA expression was also investigated in the urothelium. There was a trend of NGF increase in IC compared to NL (11.4 \pm 7.2 in IC, 7.1 \pm 4.8 in NL, $p=0.0949$).

Interpretation of results

Increased mRNA expression of Cxs in the urothelium indicates facilitation of a sensory element in bladder signalling through releasing ATP and other substances when the bladder is stretched during bladder filling¹). Cxs in the urothelium also involve in barrier function. Thus, these increases of Cxs may affect intercellular communication in the urothelium. Regarding TRP channels that are modulated by cytokines, neuropeptides and other substances, TRP channels are involved in transmission of noxious sensation²). Therefore, increased mRNA expression of TRP channels in the urothelium indicates an increase of a sensory transmission from the bladder.

Concluding message

Signal transmission of sensation in the bladder of IC patients could be changed through the increase of Cxs and TRPs in the urothelium. Further investigations of connexions and TRPs in the urothelium have a potential to develop new biomarkers to diagnose IC and effective therapeutic interventions for IC patients.

References

1. Connexins: Sensors of epidermal integrity that are therapeutic targets. FEBS Letters 588 (2014) 1304–1314
2. TRP channels and analgesia. Life Sciences 92 (2013) 415–424

Figure 1 mRNA expression of connexins

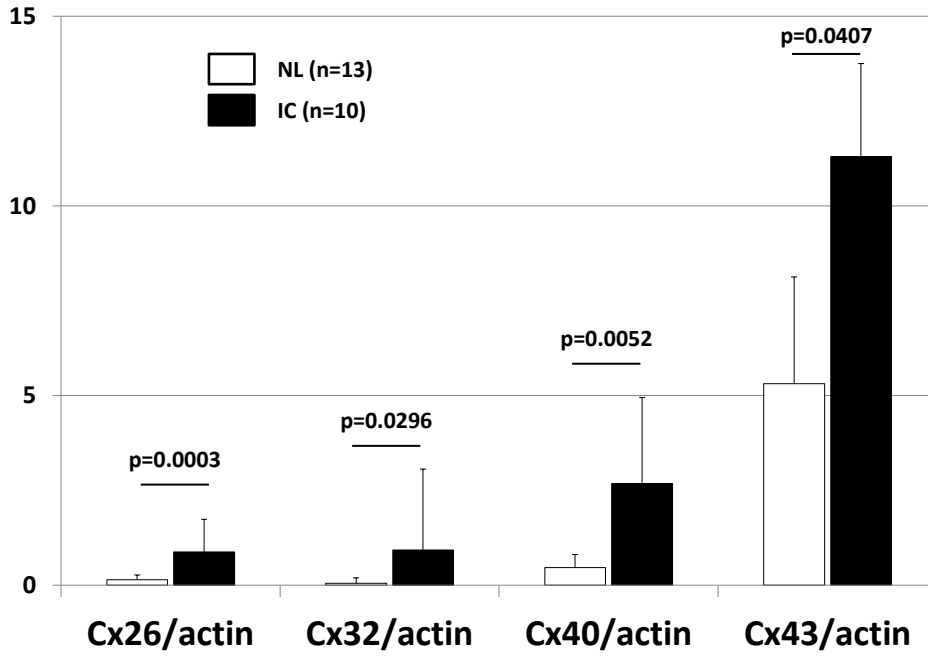
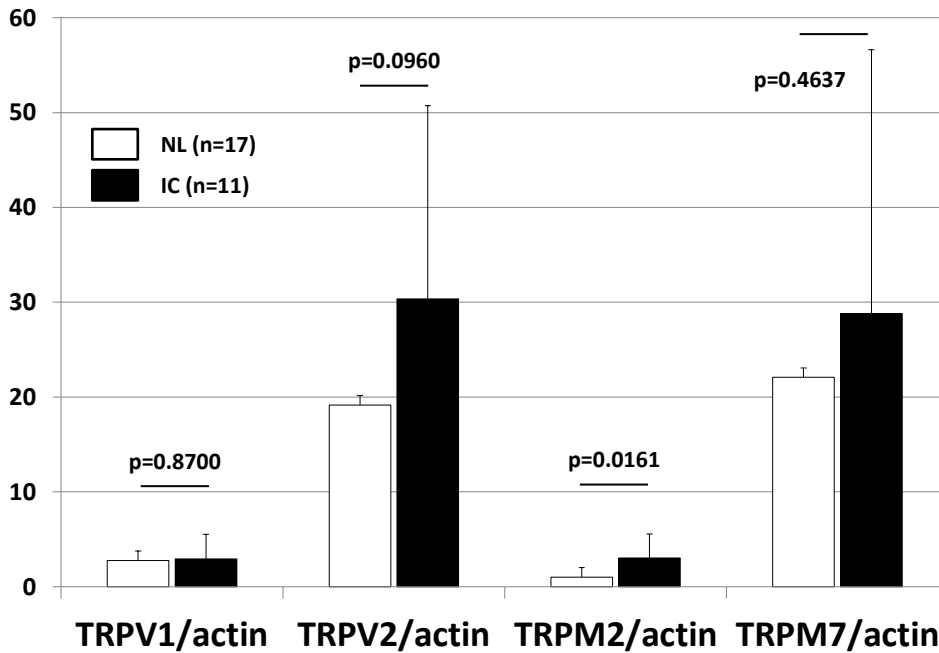


Figure 2 mRNA expression of TRPs



Disclosures

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