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THE EXPRESSION OF TRANSIENT RECEPTOR POTENTIAL (TRP) V4, A1, AND V1 IN THE HUMAN BLADDER MUCOSA OF NORMAL AND BLADDER OUTLET OBSTRUCTION. - A NOVEL MECHANISM IN THE OBSTRUCTION-INDUCED BLADDER OVERACTIVITY-

Hypothesis / aims of study
Transient receptor potential (TRP) ion channel family has unique characters of thermosensing and mechanosensing, and some of TRPs may be candidate for mechanosensor in the urinary tract (1)(2)(3). The objectives of this study are to investigate the expression profiles of TRPA1, TRPV1, and TRPV4 in normal and obstructed (BOO) human bladder mucosa, and to compare the expression profiles of TRPs in bladder mucosa and clinical parameters including lower urinary tract symptoms.

Study design, materials and methods
Urinary bladder mucosal samples from 12 patients (72.4±2.4 years old) with benign prostatic hyperplasia (BPH)/Urodynamically-proven BOO, and 8 cases of age-matched non-obstructed control were included. Quantitative mRNA expression analysis from bladder mucosa was made by real time reverse transcription-polymerase chain reaction using beta-actin as internal standard. Immunohistochemistry method was used to determine the protein expression of TRPA1, TRPV1, and TRPV4. Subjective and objective parameters, including International Prostate Symptom Score (I-PSS) and urodynamics, were analyzed to determine the correlation with TRPs expression. Statistical analysis was made using unpaired t-test and Spearman's rank-sum test.

Results
Every mRNA and protein of TRPA1, TRPV1, and TRPV4 were detected in every sample of both BOO and non-BOO patients, and TRPA1 showed highest expression of mRNA among 3 TRPs. Table shows the expression of mRNAs of TRPA1, TRPV1, and TRPV4. The expression of mRNA were higher in BOO than non-BOO in every TRP. mRNA expression of TRPA1 were 1195.45±321.82 and 56.41±20.70 in BOO and non-BOO, respectively (P<0.05). mRNA expression of TRPV1 were 47.38±12.52 and 0.65±0.40 in BOO and non-BOO, respectively (P<0.05). mRNA expression of TRPV4 were 53.43±11.62 and 10.35±8.48 in BOO and non-BOO, respectively (P<0.05). Every kind of mRNA expression of TRPA1, TRPV1, and TRPV4 showed significant positive correlation with I-PSS storage symptoms (r=0.80; p<0.001, r=0.70; p<0.05, r=0.65; p<0.01, respectively). In the immunohistochemistry, TRPA1 protein expressed mainly in the urothelium and suburothelial layer of BOO, and TRPA4 strongly expressed in the urothelium of BOO.

Interpretation of results
In BOO patients with BPH/BOO, bladder urothelium showed higher expression of TRPA1, TRPV4, and TRPV1. The functional significance of these molecules may be hypothesized by comparing with clinical findings.

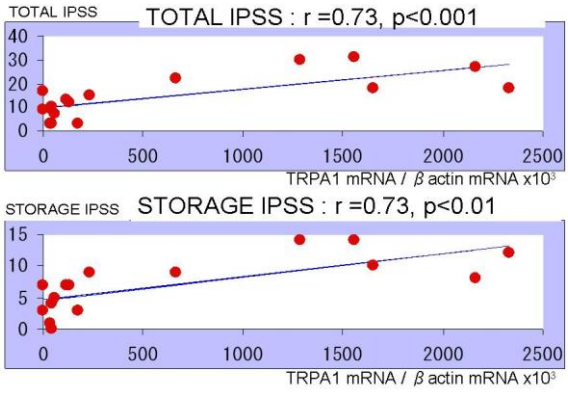
Concluding message
According to these results, TRPA1, TRPV4, and TRPV1 are candidates for mechanosensor in the human urinary bladder. Modulation of these molecules will be novel therapy for overactive bladder, and storage dysfunction.

Expression of mRNAs of TRPchannels:
Comparison between BOO and non-BOO

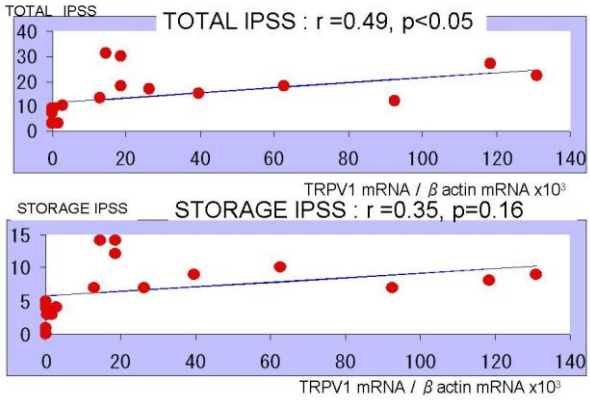
	BOO(N=12)	Control(N=7)	
TRPA1	1195.45 ± 321.82	56.41 ± 20.70	P<0.05
TRPV1	47.38 ± 12.52	0.65 ± 0.40	P<0.05
TRPV4	53.43 ± 11.62	10.35 ± 8.48	P<0.05

(TRPs mRNA/ β actin mRNA x10^3)

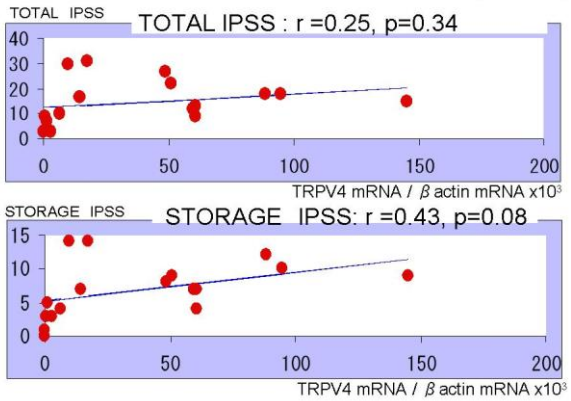
Corelation between IPSS and TRPA1mRNA expression



Corelation between IPSS and TRPV1mRNA expression



Corelation between IPSS and TRPV4mRNA expression



References

1. Urology, 69:590-595, 2007
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3. Urology 72: 450-455, 2008

Specify source of funding or grant	**None**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Ethical Committee of University of Yamanashi, School of Medicine.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**