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## VESICULAR NUCLEOTIDE TRANSPORTER (VNUT) IS A KEY MOLECULE FOR MECHANONSENSING IN THE HUMAN URINARY BLADDER: NEGATIVE CORRELATION BETWEEN VNUT EXPRESSION IN HUMAN BLADDER MUCOSA AND FIRST DESIRE TO VOID

### Hypothesis / aims of study

ATP released from bladder urothelium plays a crucial role in afferent sensation. Although there appear to be multiple ATP-release pathways, the mechanism is clearly unknown. However, a new molecule, vesicular nucleotide transporter (VNUT), has been identified in various organs that specifically release ATP (1). We have demonstrated the expression and function of VNUT in mouse bladder epithelium in mechanotransduction (2). The objectives of this study were to investigate the expression of VNUT in the human bladder and to compare the expression profiles of VNUT mRNA level and various clinical parameters.

### Study design, materials and methods

Bladder specimens were obtained from 15 patients with benign prostate hypertrophy or prostate cancer who had undergone operations at a single medical hospital. Before the operation, all patients had completed questionnaires such as the IPSS and OAB and urodynamic studies. Quantitative mRNA expression analysis of the bladder was performed using real time RT-PCR. Immunohistochemistry was used to determine the protein expression of VNUT. Age, prostatic volume, subjective parameters including I-PSS and QOL score, and objective parameters under an urodynamic study were analyzed to determine the correlation with VNUT mRNA expression.

### Results

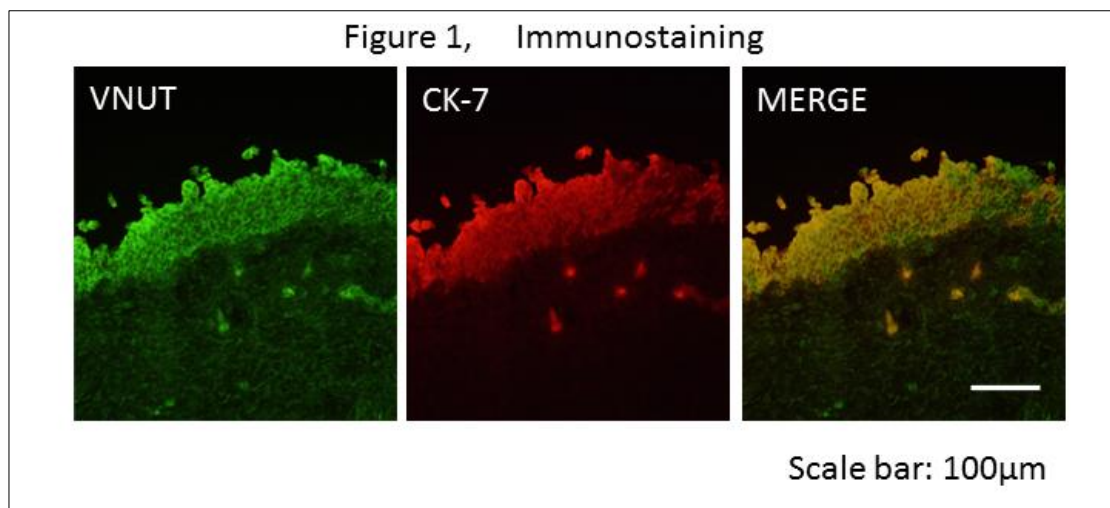
RT-PCR and immunostaining experiments showed that VNUT was highly expressed in the human bladder epithelium (Figure 1). We found that the first desire to void (FDV) was negatively correlated with VNUT expression in the human bladder urothelium ( $p < 0.05$ , Figure 2). None of the other parameters, including age, prostatic volume, maximum desire to void (MDV), IPSS, or detrusor pressure at maximum flow (PdetQmax) showed any correlation with VNUT mRNA expression.

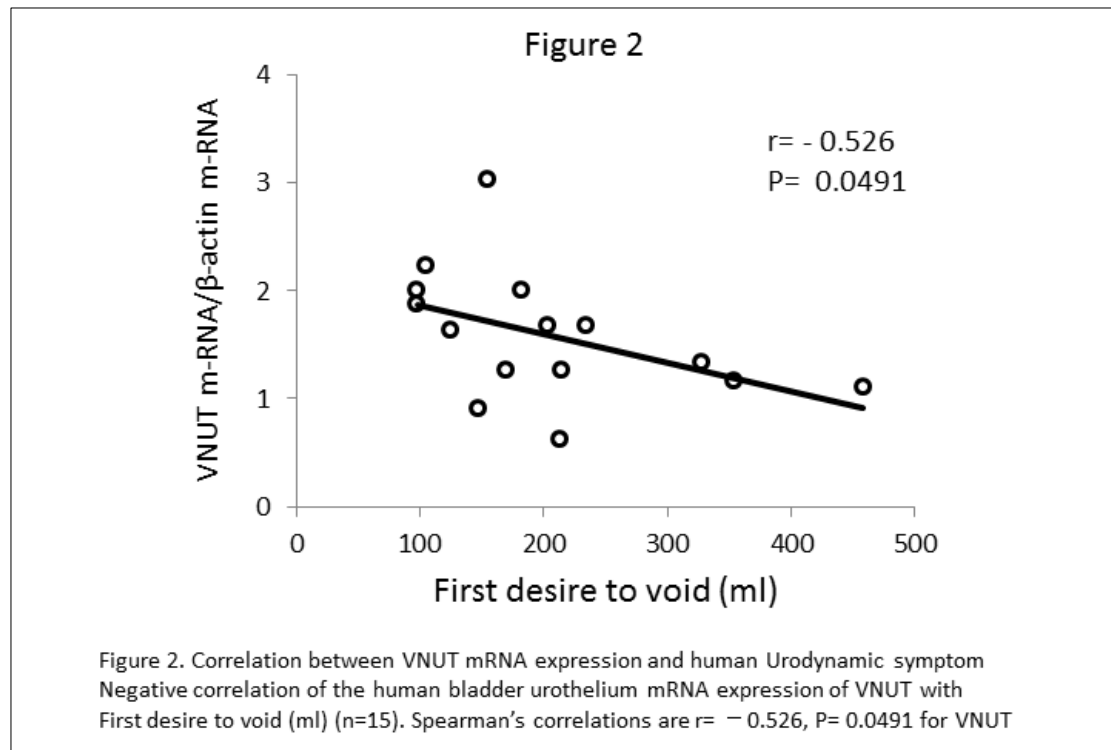
### Interpretation of results

Our results suggest that VNUT-dependent vesicular ATP exocytosis may be localized to human bladder epithelium and that ATP exocytosis is not related to pathological symptoms or functional aspects such as urine flow rate and pressure. VNUT expression and ATP exocytosis are merely considered physiological indicators for bladder sensing. However, given the limited conditions and studies available, it is difficult to discuss the role of the VNUT/ATP exocytic pathway in the human bladder.

### Concluding message

VNUT mRNA and protein are highly expressed in the human bladder epithelium. The VNUT mRNA level was shown to be negatively correlated with FDV.





#### References

1. Sawada, K. et al., PNAS, 2008
2. Nakagomi, H. et al., Poster presented at International Continence Society 41st Annual Meeting, 2011

#### Disclosures

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**Subjects:** HUMAN **Ethics Committee:** The institutional review board of Kawahara Nephro-Urology Clinic(#62) **Helsinki:** Yes  
**Informed Consent:** Yes