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Tamm–Horsfall Protein Knockout Mice Have Increased Stress Induced Micturition

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To the Editor

Tamm–Horsfall Protein (THP) is urine's most abundant protein.¹ THP has been postulated to serve as a protective factor against interstitial cystitis,² a chronic inflammation of the bladder often exacerbated by stress, that is associated with increased frequency of urination with or without pain.³

We generated THP gene knockout (THP^{-/-}) mice by the technique of homologous recombination.⁴ We examined if the absence of THP affected the frequency of urination under normal conditions and under movement induced stress. We also determined if absence of THP caused identifiable changes in bladder histology. Ten age matched, female, THP^{-/-}, and THP^{+/+} mice were selected. Each mouse was placed on Whatman grade 3 filter paper in a standard mouse cage. The mice were free to move. Food and water were given ad libitum. After 6 hr, the filter papers were examined under ultraviolet light, and spots of urine were counted. The experiment was repeated under condition of movement stress by placing the mouse cage on a rocking platform. Mice were euthanized and urinary bladders were removed. Formalin-fixed, paraffin-embedded sections of bladder were examined by a renal pathologist in a blinded manner.

Results showed that the baseline micturition frequency, in THP^{-/-} mice (2.8 ± 0.2 per 6 hr) was not different from that in THP^{+/+} mice (3.2 ± 0.2 per 6 hr; $P = 0.07$). The micturition frequency under condition of movement stress, however, was significantly higher in the THP^{-/-} mice (4.3 ± 0.4 per 6 hr) than in the THP^{+/+} mice (2.5 ± 0.4 per 6 hr; $P = 0.007$). Examination of histopathology sections of bladders showed no significant differences between THP^{-/-} and THP^{+/+} mice (Fig. 1).

Our study makes the novel observation that THP-deficient mice are more prone to stress induced increase in micturition frequency. Absence of THP might allow enhanced access of urinary toxins to local afferent neurons, resulting in interstitial cystitis.

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Fig. 1. Micturition frequency in THP^{-/-} and THP^{+/+} mice at baseline and under stress of movement.