

## OXIDATIVE STRESS INDUCED AN UP-REGULATION OF ENDOCANNABINOID SYSTEM IN RAT URINARY BLADDER

### Hypothesis / aims of study

Oxidative stress has been found to involve in bladder aging, bladder inflammation and bladder outlet obstruction. Previous research also showed that oxidative stress induced by intravesical H<sub>2</sub>O<sub>2</sub> stimulated the bladder activity with a significant reduction in the cystometric bladder capacity and inter-contraction interval, indicating that oxidative stress may induce bladder overactivity. Evidences demonstrated that endocannabinoid system played an important role in bladder overactivity. Cannabinoid receptors CB1 and CB2 are expressed in the bladder urothelium and the detrusor and are found to participate in bladder afferent signalling and cholinergic nerve activity. Inhibition of an endocannabinoid degradation enzyme fatty acid amide hydrolase (FAAH) with an increased level of endocannabinoids has been shown to reduce urinary frequency in normal rats, indicating a significant role played by the endocannabinoid system in normal micturition.

Recent reported findings indicated a close correlation between endocannabinoids and oxidative stress in some organs. Such correlation between endocannabinoid and oxidative stress might also exist in the bladder. However, no such investigation has been done in the bladder before. This project investigated the effect of oxidative stress on the endocannabinoid system in the urinary bladder.

### Study design, materials and methods

Adult female Sprague-Dawley rats were used in this experiment. Under anesthesia, the abdomen was opened and the bilateral ureters were divided to prevent the urine to enter the bladder, keeping constant concentration of the instilled solution. 0.5% hydrogen peroxide was infused continuously into the bladder of 10 animals for one hour. During infusion, the intravesical pressure was monitored continuously. After completion of H<sub>2</sub>O<sub>2</sub> infusion the bladders were obtained. Then the expression of COX-2, FAAH, CB1 and CB2 in the urothelium and detrusor was measured with real-time PCR for mRNA and western blotting for protein expression. Control group received intravesical normal saline instillation (n=10).

### Results

Our results found that COX-2 expression in both urothelium and detrusor was increased following H<sub>2</sub>O<sub>2</sub> instillation (Fig1), indicating that inflammation occurred following H<sub>2</sub>O<sub>2</sub>-induced oxidative stress. The expression of FAAH, CB1, CB2 was all increased in both urothelium and detrusor after H<sub>2</sub>O<sub>2</sub> instillation. Urothelial CB2 expression was more prominently enhanced.(Fig 2,3,4)

### Interpretation of results

Our results showed that oxidative stress induced an up-regulation of endocannabinoid system in rat urinary bladder. A close correlation exists between endocannabinoids and oxidative stress in the urinary bladder.

### Concluding message

This study clearly demonstrates that endocannabinoid system plays a significant role in the response of the bladder to oxidative stress. Endocannabinoid system might be a promising therapeutic target in treating oxidative stress-related disorder of the bladder.

Fig.1

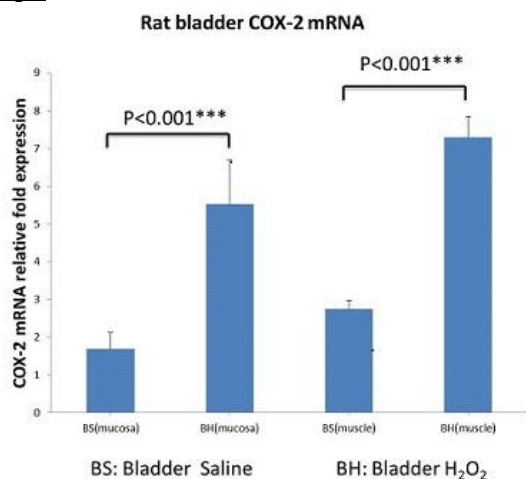


Fig.2

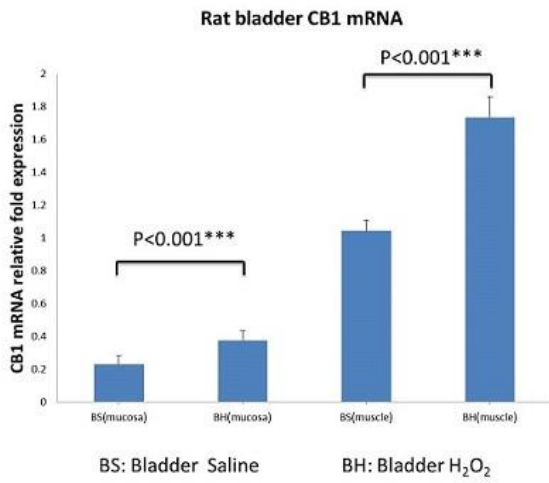


Fig.3

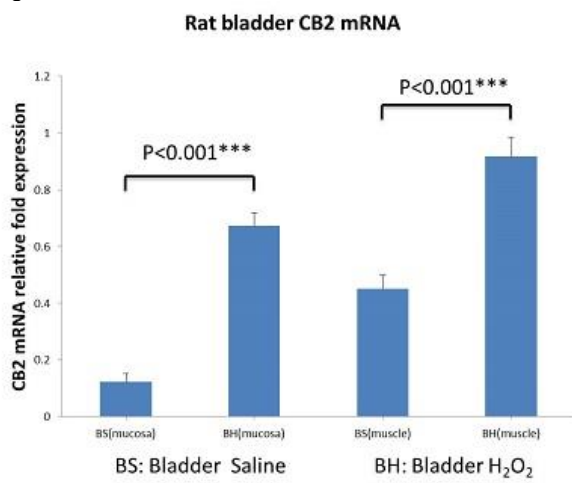
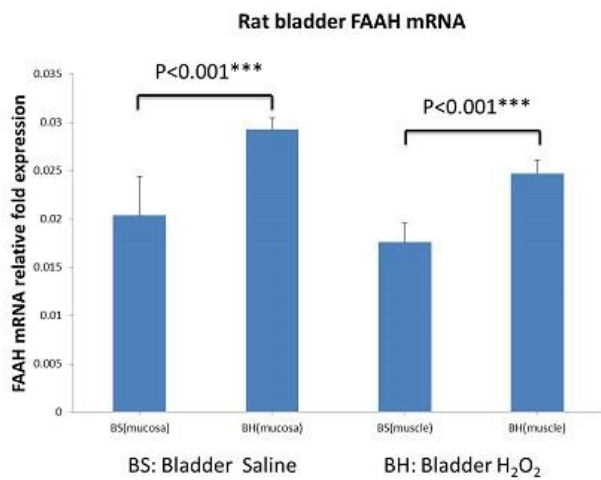


Fig.4



Disclosures

**Funding:** Taipei Veterans General Hospital **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Taipei Veterans General Hospital