500

Tempest H[1], Sellers L[2], Dixon A[1], Turner W[3], Ferguson D[1]
1. Department of pharmacology, Cambridge, 2. Babraham Institute, Babraham, 3. Addenbrookes Hospital, Cambridge

CHANGES IN GENE AND PROTEIN EXPRESSION IN INTERSTITIAL CYSTITIS

Aims of Study

It has been proposed that epithelial sodium channels (ENaCs) and $P2X_3$ receptors are involved in the sensory system of the urinary bladder. In human urinary bladders it has been shown that there are ENaCs in the urothelium, which are comprised of three subunits, alpha, beta and gamma (α, β, γ) (1). In rabbit bladders the ENaCs have been shown to be mechanosensitive, having the ability to change their sodium transport properties following small changes in hydrostatic pressure, as might occur in normal bladder filling and emptying (2).

The bladder urothelium is also known to release ATP in response to stretch (3). The release of ATP and subsequent activation of $P2X_3$ receptors is thought to play a part in bladder nociception. This was demonstrated in $P2X_3$ knockout mice that showed defects in nociception (4). It has also been shown recently that there was an increase in stretch induced urothelial ATP release from patients with Interstitial Cystitis (IC)(5).

IC is a chronic, severely debilitating, clinical syndrome of pelvic pain and/or urinary urgency and frequency. IC is still of unknown aetiology but the symptoms associated with it would indicate that there is a primary or secondary disruption of the sensory system.

We have therefore investigated ENaC and $P2X_3$ expression in patients with IC.

Methods

Ethical approval was obtained for this project. Normal bladder urothelium was obtained from patients undergoing cystectomy or radical prostatectomy and IC patient tissue was obtained from patients having a cystectomy for IC symptoms. The patients with IC were diagnosed using the NIDDK criteria (6).

Real-time PCR was used to investigate any differences in gene expression of the ENaC subunits and $P2X_3$ receptors.

Western blot analysis was used to investigate any protein differences of the $P2X_3$ receptor.

Results

Using real time PCR it was found that there was a decrease in the amounts of mRNA encoding for all the ENaC subunits and the $P2X_3$ receptor in IC tissue specimens compared to normal. Using western blot analysis it was noted that there was an increase in $P2X_3$ receptor expression in IC tissue specimens compared to normals.

Conclusions

This data has indicated that there are changes in gene expression of the ENaC subunits and $P2X_3$ receptor in normal verses IC human urothelium. There is also a change in protein expression of the $P2X_3$ receptor in normal verses IC human urothelium. These receptors may provide a pharmacological target for symptomatic relief of the condition Interstitial cystitis.

References

1. Expression of epithelial sodium channels in the epithelium of the human urinary bladder. *Neurourology & Urodynamics* 2002;21(4):404-405
2. Urothelial function *B.J.U.* 1999;84(3):235-42
3. ATP is released from rabbit urinary bladder epithelial cells by hydrostatic pressure changes-a possible sensory mechanism? *J. Physiol* 1997 ;505 (2):503-11.
4. Urinary bladder hyporeflexia and reduced pain-related behaviour in P2X3-deficient mice. *Nature*2000;407:1011-1015
5. Augmented stretch activated adenosine triphophate release from bladder uroepithelial cells in patients with interstitial cystitis. *J. Urology* 2001;166(5):1951-56
6. National Institute of Diabetes and Digestive and Kidney Diseases. Interstitial cystitis. *NIH* 1994 pub no. 94-3220