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THE LOCATION AND ROLE OF PROSTAGLANDIN RECEPTORS (TYPE 1: EP1) IN THE BLADDER AND URETHRA

Hypothesis / aims of study

Prostaglandins are suggested to have a role in functional bladder disorders such as the overactive bladder syndrome (OAB) [1,2]. Prostaglandins are synthesised in the bladder wall and released into the general circulation and bladder lumen. Studies have shown, that they can affect the smooth muscle to cause contraction of isolated strips or modulate spontaneous phasic activity (autonomous activity) [3]. It follows from this basic functional data, that we need to understand which of the prostaglandin receptors are responsible for muscle activation and where they are located. In this study, we explore the distribution of the type 1 prostaglandin receptor (EP1).

Study design, materials and methods

Bladders from five male guinea pigs, killed by cervical dislocation, were removed. Tissues were then fixed in 4% paraformaldehyde and processed for immunohistochemistry. Primary antibodies used were antibody to the prostaglandin type 1 receptor (EP1) and to vimentin , a marker for interstitial cells. Specific antibody binding was visualised using the appropriate secondary antibodies. A blocking peptide was used to confirm the specificity of the EP1 antibody (Figure C and D).

Results

In the lateral wall of the bladder, specific staining for the EP1-receptor was located on the surface membrane of the smooth muscle cells using confocal microscopy. In addition EP1 receptors were localised to a population of cells lying in the spaces between the muscle bundles and on the surface of the muscle bundles. These cells also stained with vimentin and can therefore be described as interstitial cells. No EP1 staining was observed in the lamina propria either on the urothelium or sub-urothelial interstitial cells (Figure A). In contrast to the distribution of EP1 in the lateral wall (Figure B) EP1 staining was detected in the umbrella cells of the proximal urethra in close proximity to the prostatic ducts (Figure A and B)

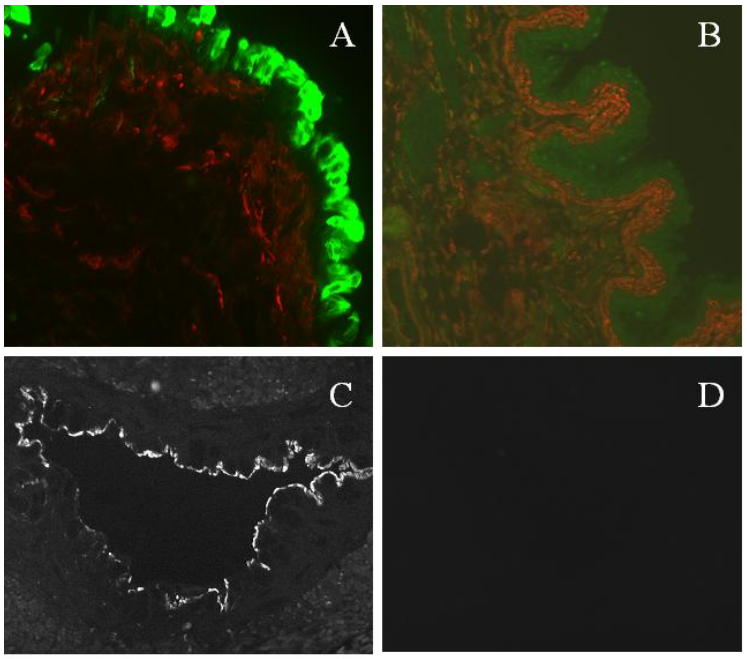

Figure A: Guinea pig urothelium of the urethra with clear EP1 immunoreactivity EP1-IR (green) Vimentin is stained red.

Figure B: Urothelium of the urethra of the same guinea pig as in A, with the absence of EP1-IR. (no green). Vimentin is stained red.

Figure C: Transection of a Guinea pig urethra at 4x enlargement with EP1 expression on the urothelium.

Figure D: Same Guinea pig Urethra as in C, pre-incubated with a blocking peptide. No fluorescence is seen so the photo is black.

Interpretation of results.

These observations demonstrate the possible operation of different systems within the bladder wall utilising prostaglandin signalling. The presence of EP1 receptors on the muscle underlies the contractions induced by prostaglandins on muscle strips. The activation of the EP1 receptors on the interstitial cells suggests an involvement in the modulation of coordinated phasic activity or in tissue remodelling. The finding of EP1 in the urothelial surface close to the prostatic duct indicates a further functional role. These receptors are in an ideal position to respond to prostaglandins in the bladder lumen, derived from the bladder wall, or from the prostatic secretions.

Concluding message

The distribution of EP1 receptors in the bladder wall as presented by our data suggest, that prostaglandins are involved in several functional processes which can represent a novel physiological system. Our data offer a fundamental base for more studies with prostaglandins in OAB.

References

1. J Urol. (2006) May; 175:1773-6
2. Rev Urol. (2002); 4; S7–S18.
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Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Animal Ethical Committy University of Maastricht**