

THE LOCALISATION OF CYCLO-OXYGENASE IMMUNO-REACTIVITY (COX I-IR) IN THE UROTHELIUM AND IN THE SUB-UROTHELIAL INTERSTITIAL CELLS OF THE BLADDER

Hypothesis / aims of study

Bladder autonomous activity has been described as part of a motor/sensory system and recently our group described the modulation of this autonomous activity by prostaglandins. Prostaglandins are synthesized by cyclooxygenases and cyclooxygenase I (COX I) is present in the bladder wall apparently associated with the urothelium and interstitial cells. However, a precise identification of structures responsible for prostaglandin synthesis in the bladder is lacking. Therefore we studied the localization of COX I in relation to one structural marker associated with interstitial cells, i.e. vimentin.

Study design, materials and methods

Bladders from seven male guinea pigs were incubated in Krebs's solution at 36°C, gassed with 95% O₂ and 5% CO₂. Tissues were then fixed in 4% paraformaldehyde and processed for immunohistochemistry. Primary antibodies used were antibody to COX I, and vimentin. Specific antibody binding was visualised using the appropriate secondary antibodies.

Results

Intense COX I-immunoreactivity (COX I-IR) was visible in the basal urothelial layer. Directly below the basal urothelium was a cell layer staining intense for vimentin. These cells were identified as sub-urothelial interstitial cells, by their long processes and vimentin-IR. Below the sub-urothelial interstitial cells were COX I positive cells in the lamina propria.

Interpretation of results

PGs are synthesised within the urothelium and lamina propria. The present observations extend this broad observation and demonstrate specifically that the expression of COX I-IR, and so the synthesis of PG, predominates within two general cell systems in the bladder wall: (i) cells within the basal and intermediate layers of the urothelium and (ii) within a population of small cells which are closely associated with a network of vimentin positive cells. These vimentin positive cells are present through out the sub-urothelial space of the lamina propria.

Like PG, NO is known to be produced by the urothelium in response to stretch. It is also known, on other cell systems, that PG production is influenced by NO and, conversely, that NO production is influenced by PGs. Thus, we have the intriguing possibility of complex signalling interactions within the basal layers of the urothelial epithelium in response to stretch.

Concluding message

There are several complex signalling systems operating within the bladder wall. These signals act within cells systems that interact between the urothelium, interstitial cells, muscle, sensory fibres and intra-mural ganglia. This study points out that the basal urothelial layer is capable of producing prostaglandin. This layer lies in close contact with the sub-urothelial interstitial cells.

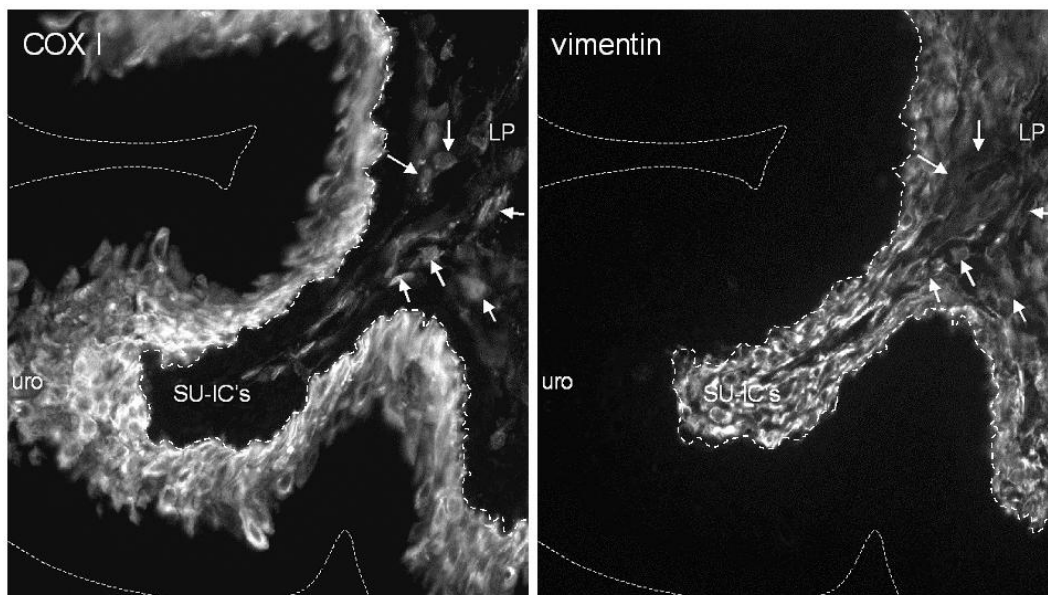


Figure 1. A network of vimentin sub-urothelial interstitial cells (SU-IC's) directly below the COX I-IR basal urothelial layer. Basal urothelial cells stain intensively with COX I (left panel). The edges of the urothelium (uro) are marked with dotted lines. Immediately below the basal urothelial cells are vimentin positive SU-IC's (right panel). Note the close relation between the COX I-IR basal urothelial cells and the vimentin positive SU-IC's. Below the SU-IC's are COX+/vimentin+ interstitial cells (arrows) in the lamina propria (LP).

<i>What were the subjects in the study?</i>	ANIMAL
<i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i>	Yes
<i>Name of ethics committee</i>	The Institutional Animal Care and Use Committee of Maastricht University
