

## **C-KIT POSITIVE STAINING IN THE SUPERFICIAL LAYERS OF THE HUMAN URINARY BLADDER.**

### Hypothesis / aims of study

There is growing interest in the possible existence of interstitial cells in the bladder wall. There is some controversy regarding the cells involved and their location. The aim of this study was to identify interstitial cells within the superficial layers of the human bladder and to assess their distribution.

### Study design, materials and methods

In the gut interstitial cells display c-Kit (stem cell factor). Therefore an anti-body to stem cell factor (CD117) was used to identify immunoreactive cells in the bladder wall.

Samples of human bladder were obtained with ethical approval. Pieces of the lateral wall and dome were taken from 5 patients undergoing radical cystectomy surgery for transitional cell carcinoma. Tissue was taken from sites well removed from the tumour. Samples of the lateral wall were also taken from the bladder of guinea pigs (n=6) killed by cervical dislocation. A standard immunoperoxidase staining was performed using the avidin-biotin method with diaminobenzidine (DAB) used as the chromogen.

### Results

In the human tissues CD117 positive cells were seen in the basal layer of the urothelium but not in the intermediate or superficial layers. These cells formed a continuous layer of strongly positive cells in tissue from the lateral wall. In tissues from the dome, CD117 cells were also present, but the staining was less intense. In the lamina propria of the lateral wall there were a small number of CD117 positive cells. Two cell types were noted: spindle shaped cells with fusiform bodies and round cells with round nuclei. Neither of these cell types had any obvious direct points of communication with other CD117 positive cells. It is possible that the round cells are mast cells since they are known to express CD117, are spherical with round nuclei.

In the guinea pig tissues a similar pattern of CD117 staining was seen, with positive cells in the basal urothelium and dispersed in the lamina propria. These basal urothelial cells also stained intensely with an antibody to neuronal nitric oxide (nNOS) suggesting that they are capable of producing nitric oxide.

### Interpretation of results

There are three reported studies which have attempted to describe interstitial cells in the human bladder<sup>1-3</sup>. All of these studies reported c-Kit positive cells associated with the muscle layer. However, only one study reported c-Kit positive cells suburothelially<sup>1</sup>. In the other two studies no superficial c-Kit cells were reported<sup>2, 3</sup>. The present observations indicate the presence of a small number of CD117 positive cells in the lamina propria of the lateral wall some of which may be interstitial cells. The varying data from these studies may result from a combination of the different antibodies used, the alteration of antigenic sites by the fixation process or differing sub-classes of interstitial cell types with their own similar but individual antigenic sites.

The most striking observation in this study was the positive staining seen in the basal urothelium, being light in the dome and more pronounced in the lateral wall. No comment was made in any of the previous studies of positive staining in the human urothelium. c-Kit positive staining was also found in the basal layer of the guinea pig urothelium. The significance of this observation and the physiological role of these cells is uncertain. These basal cells cannot be described as interstitial cells even though they are CD117 positive. The function of these cells is not known. They have the ability to synthesise NO, and therefore may have a

function associated with signalling to the outer urothelial layer or cells in the lamina propria. Alternatively, they may be precursor cells for replacement of the upper urothelial layers.

Concluding message

These results confirm the presence of CD117 positive cells in the bladder wall. They highlight the presence of a c-kit positive basal urothelial layer that requires more investigation.

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