**384**

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# INTERSTITIAL CELLS IN THE BLADDER WALL IDENTIFIED BY AN ANTIBODY TO THE C-KIT RECEPTOR ACK-2.

Hypothesis / aims of study

The presence and physiological role of interstitial cells in the bladder remains controversial. The aim of the present study was to determine which cells in the bladder wall of the guinea pig express epitopes marked by the c-Kit antibody ACK-2 and to see if these cells are similar to those described as ICCs by elevations in cGMP.

Study design, materials and methods

Cells, similar to interstitial cells of Cajal (ICCs) in the gut, were first identified in the bladder wall by their response to nitric oxide donors with a rise in intracellular cGMP (1). The physiological role of these cells remains known. In the gut, the identification of and functions of ICCs was advanced by the discovery that these cells express the proto-oncogene c-kit which encodes for a membrane bound protein c-Kit. The extra-cellular domain of c-Kit is a receptor for stem cell factor (Steel Factor) (2). Antibodies to c-Kit have been used to identify ICCs and study their distribution in the gut. However, not all c-Kit antibodies identify ICCs. The most widely used marker is an antibody raised to a cloned section of the receptor: ACK-2 (2) (e-Bioscience Cat No 14-1172). For ACK-2 characterization bladders from female guinea pigs were removed and cryo-fixed (n=8). Procedures to elevate cGMP and stain for cells responding with rises in cGMP were the same as those described previously (1).

Results

Two populations of ACK-2 positive cells were found in the bladders of the guinea pig. The most extensive staining was seen on small cells in the basal urothelium which appear to send processes along the basement membrane. These cells are distinct from the large urothelial cells and the superficial umbrella cells. Approximately 80% of the cells in this layer appeared to stain with ACK-2. In response to NO donors these cells do not demonstrate a rise in cGMP while umbrella cells, cells in the sub urothelial layer, on the surface of the muscle trabeculae and lying between muscle cells are positive. The sub urothelial cell stain positively with antibodies to neuronal nitric oxide synthase. A second much smaller population of positive cells was found in the suburothelial layer and lying between the muscle bundles.

Interpretation of results

From these observations it is clear that the antibody ACK-2 targets specific populations of cells in the wall of the guinea pig bladder. The discovery that the most wide spread staining with this antibody is located in the basal layer of the urothelium is a new and interesting observation. It is possible that these cells represent a population of urothelial stem cells which may be there to replace cells lost into the bladder lumen. However, the finding that they express NOS and do not signal using cGMP suggests that they may have additional and specific functions.

Concluding message

It can be speculated that these cells may be involved in the signalling processes within the urothelium that sense bladder wall stretch and deformation.

References

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