

DISTRIBUTION OF B-ADRENOCEPTOR SUBTYPES IN SUBUROTHELIAL INTERSTITIAL CELLS OF THE HUMAN URINARY BLADDER

Hypothesis / aims of study

Recent interest of bladder physiology has focused on the interstitial cells of the urinary bladder. These cells, often termed myofibroblasts, microscopically have been observed in suburothelial layer immediately beneath urinary bladder urothelium, further, also observed between detrusor muscle bundles. They play important roles in physiology of the bladder function via suburothelial afferent nerves or detrusor smooth muscles [1]. In humans, recent findings have shown that suburothelial interstitial cells express muscarinic receptors and purinoceptors; however, it has been no evidence whether these cells express β -adrenoceptors (ARs). The aim of this study was to investigate the distribution of β -AR subtypes, especially β_3 -AR, in these cells of the human urinary bladder by immunohistochemistry.

Study design, materials and methods

The human urinary bladder specimens were collected from patients undergoing total cystectomy for bladder carcinoma. For immunohistochemistry, paraffin sections of the urinary bladder were taken from macroscopically and histologically normal areas of formalin-fixed specimens. Deparaffinized and rehydrated sections were pretreated to unmask epitopes, and to block endogenous peroxidase activity. After incubation with primary antibodies for β_1 -, β_2 - and β_3 -AR, the slides were incubated with secondary antibodies. As a marker for cells of mesenchymal origin, polyclonal rabbit antibody to the human vimentin intermediate filament subunit and C-kit receptor antibody were used. The antigen-antibody reaction was visualized by 0.01 % 3,3'-diaminobenzidine tetrahydrochloride. All sections were counterstained with Mayer's haematoxylin, and mounted under coverslips. Immunohistochemical staining of β_1 -, β_2 - and β_3 -AR was recorded as positive or negative. A sample was considered negative when immunostaining of the cells was the same as the negative control.

Results

The distribution of β_1 -, β_2 - and β_3 -AR, as defined by positive staining, was observed in suburothelial interstitial cells of the human urinary bladder. Furthermore, its distribution was also observed in interstitial cells between detrusor muscle bundles. These positive cells had a fusiform (spindle-shaped) body with dendritic processes at each pole (bipolar) or along the side of the cell body (multipolar). They had large oval nuclei with dispersed chromatin and a single nucleolus. Positive staining for β_1 -, β_2 - and β_3 -AR was also identified in the detrusor smooth muscle cells. The negative control gave no staining of suburothelial interstitial cells and detrusor smooth muscle cells in any of the sections.

Interpretation of results

The present study provides the first evidence for the distribution of β_1 -, β_2 - and β_3 -AR subtypes in interstitial cells of the human urinary bladder. These cells have been observed in suburothelial layer immediately beneath urinary bladder urothelium, further, also observed between detrusor muscle bundles. Our recent findings also showed that β -AR subtypes were functionally expressed in human urinary bladder urothelium [2]. β -ARs existing in the urothelial cells or suburothelial interstitial cells may play important roles in physiology of the bladder function via suburothelial afferent nerves or detrusor smooth muscles.

Concluding message

This study showed distribution of β_1 -, β_2 - and β_3 -AR in suburothelial interstitial cells, further, also between detrusor muscle bundles of the human urinary bladder. However, further studies may be needed to clarify the functional role of β -ARs in interstitial cells of the human urinary bladder.

References

1. Nat Clin Pract Urol (2005) 2:546-554
2. Naunyn Schmiedeberg Arch Pharmacol (2008) 377:473-81

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Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	The ethics committee of Hamamatsu University School of Medicine
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes