409

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SIMILITUDE BETWEEN BLADDER HUMAN UROTHELIUM AND STOMACH EPITHELIAL TRPV1 EXPRESSION.

Hypothesis / aims of study

Gastrocystoplasty has been popularised in the last two decades as a potential alternative method to bladder augmentation. It has been suggested that the use of stomach avoided the metabolic problems of urological reconstruction surgery (post-augmentation stones, infection, mucus and metabolic acidosis) and offered functional advantages (1). TRPV1 (transient receptor potential vanilloid type 1), also known as vanilloid receptor 1 (VR1), is widely expressed by primary sensory nerves of the lower urinary tract and seems to be involved in the regulation of normal and pathological voiding reflex. Recently TRPV1 has also been showed in normal human bladder urothelial cells providing the evidence of complementary role of epithelial TRPV1 in the regulation of the lower urinary tract (2). We investigated the potential similitude between the bladder urothelial cells and the human stomach epitelium cell types expressing TRPV1.

Study design, materials and methods

Specimens from normal bladders (10 subjects, mean age 61 yrs.) were obtained by multiple cold cup or by full thickness biopsies. Full thickness gastric parietal fragments were obtained from the operative specimens of patients undergoing gastrectomy for gastric cancer or gastric ulcer (12 patients, mean age 59 years). Specimens were taken in the gastric body on the large curvature at least 7 cm far away from the neoplasm. Gastric mucosa appeared normal at macroscopic evaluation. Immunohistochemistry, by using three different commercially available anti-capsaicin-antibodies, *in situ* hybridization and Western Blot analysis were performed on samples obtained. As controls some series were treated by omitting the primary antibodies or by pre-treatment with the epitopes for the TRPV1.

Results

In normal bladder specimens the urothelium was always labelled and the labelling was intracytoplasmatic, often slightly granular. Although all cell types were stained, the superficial cells showed a higher intensity than the basal and club-shaped ones, with all the three antibodies used. In controls, Western Blot analysis recognised two thick, intensely stained bands, with a molecular weight of approximately 100 and 95 kDa.
In the stomach, TRPV1-labelling was found in the parietal cells at the level of intracytoplasmatic spaces, granules matching mitochondrial features and distribution. Immunolabelled neurons and nerve fibres were also seen (similar findings were recorded in the bladder wall), the latter numerous in submucosa and mucosa and often ending close to the parietal cells. TRPV1 presence was confirmed by Western Blot analysis, which recognised one thin band with a molecular weight of approximately 97 kDa, and by *in situ* hybridization.

Interpretation of results

The present study confirms that the normal human bladder urothelium expresses the TRPV1. The implication of these findings is that TRPV1 can not be considered anymore a “specific neuronal sensory-receptor” only.
This study immunohistochemically demonstrated the presence of TRPV1 in the human stomach, and, to our knowledge, this is its first report in man. The labelling is very intense in parietal cells and it could suggest that TRPV1 expression might be related to the specific function of this cell type, i.e. the HCl secretion. This hypothesis appears even more likely if we consider that: i) TRPV1 is a non-selective cation channel involved either in Ca^{+2} binding or mobilization [29], ii) Ca^{+2} is stored in the mitochondria of the parietal cells and is necessary to produce HCl, iii) mitochondria are involved in cation production, and, iv) TRPV1 is activated by low pH as well as by capsaicin [27,30,31]. As a whole, the mitochondrial TRPV1 could be

one of the steps of an intracellular circuit of auto regulation of HCl production by the parietal cells.

Concluding message

Both the human bladder urothelial cells and epithelial cells of the stomach expressed TRPV1. The localisation of labelling is often intracytoplasmatic and appeared granular. For our best knowledge this is the first observation in humans an further studies are mandatory to understand the functional role of TRPV1 in urothelium as well as in the parietal cells of stomach. Finally, our findings could support the use of stomach in the bladder augmentation and justify better functional results when compared with other gut substitutes (ileum and colon).

References

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