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TRANSIENT RECEPTOR POTENTIAL VANILLOID TYPE 1 (TRPV1) MORE THAN A FUNCTIONAL SENSORY RECEPTOR: TRPV1 EXPRESSION CHANGES FROM NORMAL UROTHELIUM TO TRANSITIONAL CELL CARCINOMA OF HUMAN BLADDER.

Hypothesis / aims of study

Several studies suggested that the transient receptor potential vanilloid type 1 (TRPV1) is involved in the control of cell growth, transformation and death (1). The present aim was to investigate TRPV1 expression changes from normal urothelium to transitional cell carcinoma (TCC) of human bladder.

Study design, materials and methods

Specimens from normal bladder (13 subjects, mean age 62 yrs.), superficial TCC (n=16, mean age 62,4 yrs.) and muscle invasive bladder cancer (n=12, mean age 67 yrs), were obtained by multiple cold cup biopsy and full-thickness biopsy during open surgery. All the specimens were processed for hematoxylin-eosin staining, immunohistochemistry and Western Blot analysis by using three different commercially available anti-capsaicin-antibodies. As controls some series were treated by omitting the primary antibodies or by pre-treatment with the epitopes for the TRPV1.

Results

In controls, the urothelial cells showed an intracytoplasmatic labelling whose intensity was higher in the superficial cells than in the basal and club-shaped ones. In the superficial TCC, the urothelium showed a reduced labelling intensity. In the muscle invasive TCC, a very light labelling was occasionally detected in scattered superficial cells and no labelling was present in the less differentiated cells as well as in those had invaded the muscle. In controls, Western blot analysis recognized two thick, intensely stained bands, with a molecular weight of approximately 100 and 95 kDa. In all superficial TCC there were two bands similar to control ones and in the muscle invasive two very thin, lightly stained bands. No band was detected in the patients staged as pT4.

Interpretation of results

The present study confirms that the normal human bladder urothelium expresses the TRPV1 and demonstrates that in the transitional cell carcinoma (TCC) the expression of this receptor decreases progressively with the increase of stage/grade and cell de-differentiation. Indeed, while TRPV1 expression was slightly reduced in those cases staged as superficial TCC, the receptor was rarely detected or completely absent in muscle invasive TCC. The implications of these findings are twofold: first, these data demonstrate and confirm that TRPV1 can not be considered anymore a "specific neuronal sensory-receptor" only; second, the loss of expression in high stage – high grade TCC suggests that the receptor is linked to cell growth and differentiation.

Concluding message

These data seem to show that TRPV1 could have a role in cell growth and differentiation control, and suggest the hypothesis that this receptor might be used as marker for tumour progression or as target for intravesical chemotherapy.

Reference

1. Guzman M, Sanchez C and Galve-Roperh I. Control of the cell survival/death decision by cannabinoids. J Mol Med 2001; 78: 613