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THROMBOXANE A2 INDUCES CONTRACTION OF HUMAN PROSTATE SMOOTH MUSCLE BY RHO KINASE- AND CALMODULIN-DEPENDENT MECHANISMS

Hypothesis / aims of study

Thromboxane A2 (TXA2) induces contraction in different smooth muscle types via its receptor (TXA2-R). However, the role of TXA2 in regulation of prostate smooth muscle tone has not been investigated to date. The aim of the current study was to investigate whether TXA2 induces contraction of human prostate tissue.

Study design, materials and methods

After ethical approval, prostate tissue was obtained from 37 patients undergoing radical prostatectomy. Effects of the TXA2 analogue U46619 in isolated human prostate preparations was studied in organ bath experiments with or without the Rho kinase inhibitor, Y27632, or the calmodulin antagonist W7. Expression of TXA2 synthase (TXS) and the TXA2-R were examined by Western blot analysis and immunohistochemistry. Endogenous TXA2 was quantified by enzyme immunoassay (EIA).

Results

U46619 (0.1-30 µM) induced concentration-dependent contractions of human prostate strips, with a maximum contraction of 0.426±0.144 g at 3 µM. U46619-induced prostate contraction was significantly inhibited by the Rho kinase inhibitor Y27632 (30 µM) and by the calmodulin inhibitor W7 (100 µM) (Fig A and B). TXS and TXA2-R were detected by Western blot analysis in prostate samples. As revealed by immunohistochemical stainings, the expression of TXS in prostate tissue was located to glandular cells, while the expression of prostate TXA2-R was located to smooth muscle and glandular cells. The stable TXA2 metabolite TXB2 was detected by EIA in the prostate (1.2±0.301 ng TXA2/mg prostate protein).

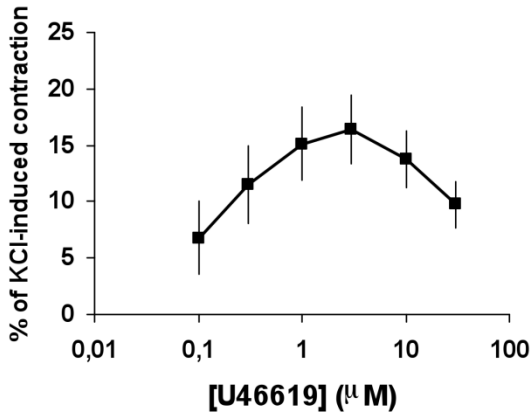
Interpretation of results

TXA2 is present in the human prostate and induces contraction of isolated human prostate tissue by activation of Rho kinase Ca^{2+}-dependent mechanisms.

Concluding message

The distribution of TXS and the TXA2-R in the human prostate suggest TXA2-mediated paracrine epithelial-stromal interactions.

A



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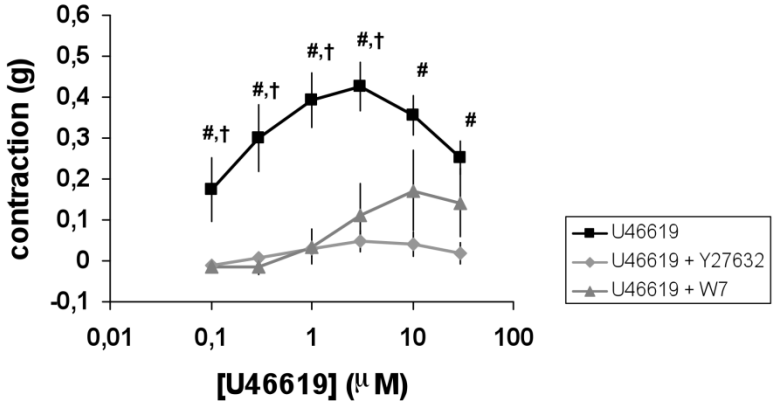

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