Kunitz Type Inhibitor (rKTI) Induces Modulation On Genes Expression Inhibits Proteasome Complex And Cause Death Of Cancer Cells

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Introduction: A recombinant protein, with inhibitory activation Factor-X, and characterized as kunitz type inhibitor (rKTI) was obtained from cDNA library of salivary gland of tick. When tested in different cell strains the protein showed apoptotic activity on tumoral cells (human melanoma Sk Mel-28, pancreatic adenocarcinoma Ma Paca-2). rKTI doesn't show cytotoxic activity on normal cells (Fibroblasts and HUVECs). **Objectives:** The aim of this study is to evaluate influence of rKTI on gene expression and on microenvironment of cells cancer before and after treatment. **Methods:** Cell death was evaluated by Flow Cytometry. Changes in gene expression were evaluated by microarray, the release of cytokines was evaluated by ELISA and the protesomal activity was assessed by Fluorimetry. **Results:** The obtained data showed that the rKTI alters genes expression of both cell lines. The cell microenvironment showed changes on levels of VEGF, IL-6 and IL-8. The rKTI also demonstrating to inhibit tryspsin-like activity of Proteasome. **Discussion:** The genes altered after treatment seems to be involved in cell-cycle control. One of genes identified (PSMB2) codified a Proteasome subunit (beta-2 subunit). Furthermore, the treatment with rKTI decreases the release of interleukins to cell microenvironment.**Conclusion:** Our hypothesis is that rKTI inhibits the activity of proteasome (thought induces an increase in the expression of the gene PSMB2). This disrupts cell cycle control, prevents the activation of NF*kappa*B, and reduces the release of interleukins causing death of tumor cell .

Keywords: rKTI, Microenvironment, Microarray, Apoptosis, Proteasome

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