Hormonal regulation of human tissue kallikrein 9 in human cancer cell lines

Nader Memari, Linda Grass, Iacovos P. Michael, Nikolaus P. Fountas, and Eleftherios P. Diamandis

Department of Laboratory Medicine and Pathobiology, Faculty of Medicine, University of Toronto and Mt Sinai Hospital, Toronto, ON, M5G 1X5, Canada

ABSTRACT:

Human tissue kallikreins (KLKs) are a group of 15 genes, tandemly located on chromosome 19, with considerable similarity at the gene and amino acid structure. Classical kallikreins such as KLK1 and KLK12 (also known as prostate specific antigen, PSA) are currently used as biochemical markers for diagnosis and monitoring of prostate cancer. Numerous reports indicate that many of the newly identified kallikreins are differentially expressed in ovarian, breast and prostate cancer. KLK9 (KLK9) identified in our laboratory, is one of the newly characterized members of the kallikrein gene family. Our earlier clinical studies indicate that KLK9 mRNA is differentially expressed in ovarian and breast cancer patients with KLK9-positive tumors have longer progression-free and overall survival compared to those who are KLK9-negative.

RESULTS:

• Clinical studies indicate that mRNA of many of the newly identified kallikreins is differentially expressed in ovarian, breast and prostate cancer.

• KLK9 mRNA expression is down-regulated in ovarian and breast cancer patients.

• KLK2 and KLK9 are currently used in the diagnosis and monitoring of prostate cancer. Gene expression of these two kallikreins is reported to be hormonally regulated by androgens and progesterone in human cancer cell lines.

• KLK9 gene expression in human prostate, ovarian, and breast cancer cell lines may also be under hormonal regulation.

METHODOLOGY:

• Hormonal regulation of KLK9 in LNCaP, PC-3, and PC-3 (AR6) prostate cancer cell lines, Caov-3 ovarian cancer cell line and the BT-474, MCF-7, MDA-MB-468, and BT-20 breast cancer cell lines was investigated. Cancer cells stimulated with estradiol, dihydrotestosterone (DHT), norgestrel, aldosterone, dexamethasone or ethinyl estradiol were grown until 80% confluent. Total RNA was extracted from the cell lines using Trizol reagent. 1.6 µg of RNA was reverse-transcribed into first-strand cDNA using Primers specific to KLK9. Amplification of cDNA was performed using Taq DNA polymerase. The PCR products were separated on 1% agarose gel, and photographed under UV light.

• PSA expression up-regulated by androgens and progesterone was simultaneously measured and used as a positive control.

DISCUSSION:

• Our results indicate that similar to other kallikreins KLK9 mRNA expression is regulated by steroid hormones.

• Since then numerous studies have confirmed the value of serum PSA determinations in the diagnostic and monitoring of prostate cancer patients. Recent reports indicate that KLK2 may soon find application as an additional prostate and breast cancer biomarker.

• We have recently developed anti-KLK9 specific antibodies. KLK9 protein in the supernatant of the cultured cancer cell lines will be probed using these antibodies.

REFERENCES:


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