ABSTRACT

Introduction: Secreted serine proteases such as kallikreins (KLKs) are expressed in multiple cell types and may play a role in the pathophysiology of a number of diseases. hK6 is a member of the KLK family that has been implicated in several malignancies including ovarian cancer. Local protein expression and methylation patterns have been reported in clinicopathological studies. The aim of this study was to investigate the expression and regulation of hK6 in ovarian cancer.

MATERIALS & METHODS

Cytosolic extracts from ovarian tissues were analyzed with an enzyme-linked immunosorbent assay (ELISA). Results were statistically analyzed to determine the prognostic value of hK6. Selected samples of all four types of specimens were subjected to total promoter and 6 exons were amplified and sequenced to screen for mutations. To examine the role of DNA methylation and hormonal effects on transcription, normal ovarian and ovarian cancer cell lines were treated separately with the methylation inhibitor 5'-aza-2'-deoxycytidine as well as 5 steroid hormones.

CONCORDANT EXPRESSION OF hK6 mRNA AND PROTEIN

hK6 CORRELATION WITH CA125 AND HISTOTYPE

GENOMIC MUTATION SCREENING

PROGNOSTIC SIGNIFICANCE OF hK6

Steroid Hormone

Dna Methylation

REFERENCES

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Up-regulation of the potential ovarian cancer biomarker, human kallikrein 6

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Background:

Ovarian cancer: The most lethal gynecologic malignancy for women in the industrialized countries.

Human tissue kallikreins (HKs): Potential prognostic markers

Secreted serine proteases

Concurrent upregulation of 12 HKs at mRNA and protein level

Rationale & Hypothesis:

Few studies have examined the processes responsible for the upregulation of the kallikreins in ovarian cancer.

We hypothesized that hK6 is under transcriptional regulation in ovarian cancer

Experimental Design:

1. Quantify hK6 protein expression in ovarian cancer tissues
2. Evaluate prognostic significance of hK6 protein
3. Examine KLK6 mRNA expression in ovarian cancer tissues
4. Examine relative abundance of 2 KLK6 alternative transcripts
5. Conduct genomic DNA mutation screen on KLK6
6. Examine the role of steroid hormones on hK6 expression
7. Examine the role of DNA methylation on hK6 expression

Conclusions:

1. hK6 is significantly up-regulated in ovarian cancer
2. hK6 up-regulation is concordant at mRNA and protein level
3. hK6 is under transcriptional regulation
4. No differential expression patterns of alternative mRNA transcripts
5. No genomic DNA mutations in 7 exons and 5'-flanking region sequenced
6. 2 linked SNPs exist in 5'UTR of AT1 but is not related to hK6 expression
7. hK6 expression in ovarian cancer is not under the influence of DNA methylation or steroid hormones

References:


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