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Presentation Title: Over-expression of human kallikrein 6 (hK6) protein and mRNA in ovarian carcinoma

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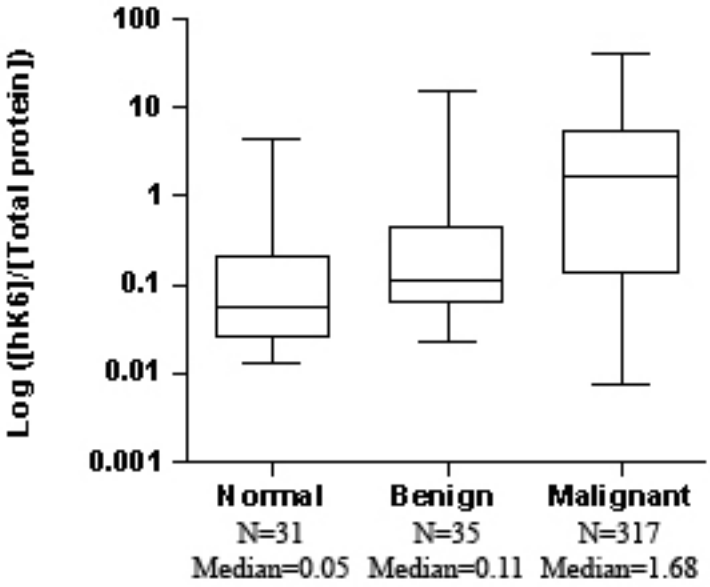
Human tissue kallikreins (hKs), a family of serine proteases, are potential cancer biomarkers that are differentially expressed in several cancer types. This study examines the expression of hK6 at both the protein and mRNA level in a large series of ovarian carcinoma tissues.
Cytosolic extracts of 317 malignant, 35 benign, and 31 normal ovarian tissues were analyzed with an hK6-specific enzyme-linked immunosorbent assay (ELISA) based on two monoclonal antibodies. Data between groups were compared using the Mann-Whitney test. The median hK6 concentration in malignant tumor tissues was approximately 34-fold higher than normal ($p<0.0001$) and 15-fold higher than benign tissues ($p<0.0001$). Figure 1 illustrates the over-expression of hK6 in malignant ovarian tumor tissues.

Fig. 1 hK6 Levels in Normal, Benign, and Malignant Ovarian Tissues (all values are expressed as [ug of hK6 per g of total protein])



We then examined if the hK6 mRNA expression correlates with hK6 protein concentration in a selected group of tissues. Ten tumor tissues were studied: 5 with the highest levels of hK6 protein expression and 5 with no hK6 expression. Total RNA from these tissues was extracted using the Trizol® reagent. Reverse transcriptase - polymerase chain reaction (RT-PCR) with KLK6-specific primers demonstrated concordance between mRNA expression and protein concentration in 9 out of 10 tumors. The tissues with high hK6 protein concentration were positive by RT-PCR and those with zero hK6 concentration were negative. One tumor had high mRNA expression but no detectable hK6 protein by ELISA. We further observed that of the 4 known transcript variants and 1 classical form of the KLK6 gene, transcript variant 2 is the predominant transcript in all 5 tumors with positive mRNA expression. This transcript lacks untranslated exon 1 and has a transcription initiation site within untranslated exon 2 of the classical KLK6 form. We conclude that the over-expression of hK6 in ovarian carcinomas is primarily regulated at the transcriptional level. The mechanisms underlying this up-regulation need to be further investigated.

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