97th AACR Annual Meeting April 1-5, 2006 Washington, DC

Abstract Number: 94

Presentation Title: The human kallikrein gene 6 (KLK6) in combination with CA125 is a more

sensitive marker for ovarian cancer than CA125 alone

Presentation Start/End

Time:

Sunday, Apr 02, 2006, 8:00 AM -12:00 PM

Location: Exhibit Hall, Washington Convention Center

Poster Section: 4
Poster Board Number: 6

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The human kallikreins are a family of 15 secreted serine proteases located on chromosome 19q13.3-13.4. Recent reports have linked kallikreins to various malignancies. The human kallikrein gene 6 (KLK6) is a newly characterized member of the human kallikrein family. Recent work has focused on the possible role of this gene and its protein product as an early predictive marker for ovarian cancer. The current marker used for detection and monitoring ovarian cancer patients after treatment is CA125. Unfortunately, this marker lacks the sensitivity and specificity to detect early stage ovarian cancer. There is an urgent need for new predictive and prognostic markers for ovarian cancer. Recent studies indicate a combination of, rather than a single biomarker will be more valuable to predict malignancy. We hypothesize the combination of both CA125 and KLK6 expression will be a more sensitive test for early detection of ovarian cancer than either marker alone. Archival formalin-fixed, paraffin-embedded primary ovarian carcinomas of different histological type, grade, stage and size of ovarian tumor were analyzed. Of the 145 cases analyzed, serum CA125 concentrations were available for 90 patients. Protein expression was observed immunohistochemically using a polyclonal hK6 antibody. Relative quantitation of KLK6 and CA125 mRNA expression was done using real-time quantitative reverse transcription -PCR. GAPDH was amplified to normalize expression of target genes. CA125 serum levels, which correlate with protein tumor expression, were elevated in 73% ovarian cancer patients. When hK6 and CA125 expression was analyzed in combination, protein levels detected 88% of patients. Elevated hK6 protein detected 16% patients that did not have elevated CA125 serum levels, 6% of these patients being Stage 1 ovarian cancers. Preliminary data indicates that both hK6 and CA125 protein expression correlates with gene expression in tumor samples. In combination, KLK6 and CA125 expression is a more specific and sensitive indicator of ovarian cancer than CA125 alone.

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