1058 Kallikrein 6 as a biomarker for the detection of metastatic cancer cells in blood of ovarian cancer patients.

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Kallikreins are a family of secreted serine proteases that have been recently discovered and seem to associate with cancer. The genetic locus of these proteases lies at 19q13.3-13.4. Human Kallikrein 6 (hK6) is a member of this protein family and it is encoded by KLK6 gene. We have previously found that hK6 is elevated in the serum of ovarian cancer patients and over-expression of hK6 tended to be greater at later stages of the disease. These findings suggest a potential role of serum hK6 concentration as a biomarker for ovarian cancer.

This present study aims to utilize KLK6 gene transcripts for the detection of disseminated ovarian cancer cells in blood. Previous studies on ovarian, prostate and breast cancer patients, using molecular markers, have detected circulating metastatic cancer cells. In some cases, the methods show high sensitivity and detect metastatic cells at a ratio of around 1 metastatic cell to 10^6 cells not expressing the marker gene.

We first identified a cancer cell line, PC3(AR6), that strongly expresses KLK6 and another cell line, ES2, that does not express KLK6. To determine the detection limit of our method we diluted KLK6 transcripts (KLK6-pBluescript plasmid) up to 1 transcript per reaction. Using KLK6 as a marker and Polymerase Chain Reaction (PCR), we were able to detect around 10 transcripts per reaction. We also diluted the PC3(AR6) cells up to 1 cell and using Reverse Transcription PCR (RT-PCR) we were able to detect less than 1 PC3(AR6) cell per reaction. We then mixed PC3(AR6) cells with ES2 cells in ratios up to $1:10^6$. Using RT-PCR, we were able to detect less than 1 PC3(AR6) cell per reaction.

We can conclude that we have developed a highly sensitive method for monitoring KLK6 mRNA and cells expressing this gene. In the future we will examine if this technology can detect circulating ovarian cancer cells for the purpose of disease diagnosis and prognosis.