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Presentation Title: Expression of human tissue kallikrein 5 in breast and prostate cancer cell lines after treatment with the demethylating agent 5-aza-2'-deoxycytidine.

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Human tissue kallikreins (KLKs) are a group of serine proteases encoded by 15 structurally similar genes that co-localize to chromosome 19q13.4. Numerous clinical studies indicate that the mRNA and protein levels of many kallikreins are aberrantly expressed in breast, ovarian and prostate cancer. Previous reports have indicated that epigenetic alterations are responsible for the reduced expression of human kallikrein 10 in breast cancer cells. For the remaining kallikrein genes, epigenetic alterations have not been examined as a potential mechanism underlying their reduced expression in numerous malignancies. Biocomputational analysis revealed putative CpG islands in the 5' upstream sequence of KLK5 indicating that genomic DNA methylation and other epigenetic alterations could contribute to silencing KLK5 gene expression in cancer cell lines. In an effort to investigate if epigenetic alterations play in the reduced expression of KLK5 in cancer cells, we examined the expression profile of KLK5 in human breast and prostate cancer cells exposed to the demethylating agent, 5-aza-2'-deoxycytidine (5-aza-dC). The following cells lines were treated: breast cancer cell lines: BT-474, MCF7, T-47D, ZR-75-1, prostate cancer cell lines: LNCaP, PC-3, and cervical cancer cell line: Hela. Protein expression were identified using a highly sensitive and specific immunoassay for hK5. Up-regulation of KLK5 mRNA levels was observed by reverse transcriptase polymerase chain reaction (RT-PCR). Changes in hK5 expression were seen with all breast cancer cell lines tested. For example, the concentration of hK5 protein secreted by MCF7 was 0.16 µg/L, but was increased to 0.66 µg/L upon treatment with 10µM of 5-aza-dC. No differential expression of KLK5 was apparent in any of the other cell lines tested. Our results indicate that epigenetic alterations may be responsible for the reduced expression of KLK5 in breast cancer cell lines.

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