

KALLIKREINS AS CANCER BIOMARKERS.**E.P. Diamandis.**

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Introduction: Until recently, 3 human kallikrein genes were recognized, the pancreatic/renal kallikrein (hK1, encoded by the KLK1 gene), human glandular kallikrein 2 (hK2, encoded by the KLK2 gene) and human kallikrein 3 (hK3, encoded by the KLK3 gene; hK3 is better known as prostate-specific antigen, PSA). PSA and hK2 have already found important clinical applications for diagnosis and monitoring of prostate cancer.

Methods: By using bioinformatic approaches and classical gene cloning methodologies, we have recently succeeded in cloning new kallikrein genes and in mapping other serine proteases at the human chromosomal locus 19q13.3-q13.4. We have then attempted to construct the complete kallikrein gene locus on chromosome 19.

Results: We have constructed the first detailed map of the human kallikrein gene locus which now contains at least 15 genes. All genes are present at this locus in tandem without any intervention by non-kallikrein genes. All genes encode for apparently active serine proteases and they share significant similarities at both the amino acid and nucleotide level. All genes are composed of 5 coding exons of comparable length and the intron phases in all these genes are fully conserved. These data suggest that the 15 genes at this locus comprise a family that originated by gene duplication. Gene expression studies indicate that some of these genes are preferentially expressed in certain human tissues. Preliminary data indicate that at least some members of this gene family may constitute new cancer biomarkers.

Conclusions: In addition to PSA and hK2, many other homologous genes have been discovered which encode for secreted proteins. Some new kallikrein gene members have potential as biomarkers for certain types of cancer.