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Presentation Title:	**Identification of single nucleotide polymorphisms in the human kallikrein locus: Potential association with cancer susceptibility**
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The human kallikrein family is composed of 15 genes arranged in a contiguous cluster on chromosome 19q13.4. These genes show evidence for hormonal regulation, as well as broad tissue expression, especially in endocrine tissues. Numerous members of the family have shown clinical use as cancer biomarkers. Human Kallikrein 3 (hK3), also called prostate specific antigen (PSA), and hK2 are valuable biomarkers for prostate cancer, hKs 6, 7, 8, 10 and 11 are emerging biomarkers for ovarian cancer, and hKs 5 and 14 are biomarkers for breast cancer. Beyond their uses in cancer detection, expression levels of some kallikrein genes have been linked with cancer prognosis. High expression of hK3 has been associated with increased survival in breast cancer, and hKs 11 and 13 show promise as favourable prognostic markers for ovarian cancer. The role of SNPs in kallikrein expression levels has already been established, with SNPs in KLK3-associated Androgen Response Elements showing direct effects on protein expression levels, and SNPs in the KLK2 gene also showing a relationship with serum hK2 levels.
In this study, we set out to characterise all the Single Nucleotide Polymorphisms (SNPs) found in the human kallikrein locus, an area of ~400kb in length. We classified each SNP by its location, be it in an exon, intron, conserved or putative regulatory region, and attempted to elucidate any effects each polymorphism would have.
Of the 323 validated SNPs in the kallikrein locus, 248 were found to be within the boundaries of individual kallikrein genes. Of these, 189 were in introns, 33 were in exons, 25 in untranslated regions, and 1 at a splice junction. Of the 33 validated exonic SNPs, 15 do not lead to an amino acid change, and 18 do. These are as follows: hK1: Arg77His, Glu145Gln, Lys184Glu, Val193Glu; hK2: Arg250Trp; hK3: Glu32Lys, Leu132Ile; hK4: Ser22Ala (within the signal peptide), His197Gln; hK5: Gly55Arg (within the propeptide), Ile172Val, Ser210Thr; hK10: Ser50Ala, Leu149Pro; hK11: Gly17Glu (within the signal peptide), Arg134Cys; hK14: His29Tyr; hK15: Pro134Leu.
5 of the above changes lead to amino acids of similar character. 10 result in a significant change of character, and the remaining 3 changes would have strong structural implications.
Several of the predicted primary sequence changes could alter the enzymatic activity of the encoded proteins. As human kallikreins have already been shown to be associated with cancer prognosis, individuals possessing these polymorphisms may show significant differences in cancer predisposition. In addition, SNPs located outside genes could affect their expression through altered regulatory effects. The activity of these kallikrein enzyme isoforms merits further study in the future.

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