
THE NEW HUMAN KALLIKREIN GENE FAMILY ON CHROMOSOME 19Q13.3-Q13.4 AND ASSOCIATION TO VARIOUS TUMOURS

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Objectives: Characterization of the human kallikrein gene locus, and studying the relation between members of this family and various types of malignancies.

Methods: Restriction analysis, end sequencing, long PCR, gene prediction programs, were used to construct the human kallikrein gene locus and to identify new kallikrein genes. Gene expression was compared between normal and malignant tissues of various origins by PCR.

Results: We constructed the complete human kallikrein gene locus, with one base accuracy, containing 14 different genes, and identified 6 new kallikreins. These genes are expressed in diverse tissues and that most of them are regulated by steroid hormones. PSA and KLK2 are established biomarkers for prostatic carcinoma. KLK4 is a new cancer biomarker with tissue-restricted (prostatic) specificity, which is differentially expressed between normal and malignant prostatic and ovarian tissues. KLK-L2 is dramatically up-regulated in a large subset of ovarian carcinomas. zyme is up-regulated in primary breast and ovarian carcinomas human stratum corneum chymotryptic enzyme and neuropsin were found to be up-regulated in a subset of ovarian carcinomas. NES1 is down-regulated in breast carcinomas and appears to be a novel tumor suppressor. KLK10 expression is down-regulated in testicular carcinomas and in more aggressive forms of prostate cancer. KLK-L5 and KLK-L4 are down-regulated in primary breast carcinomas.

Conclusions: Many members of the new human kallikrein gene family are associated with carcinogenesis. Since all these genes encode for secreted proteins, they may have value as novel biomarkers for diagnosis, monitoring and prognosis of various carcinomas.