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Hormones and Cancer II Poster Session, Thursday, 6/22, Board 156

KLK-L5 Is a New, Hormonally Regulated, Member of the Kallikrein Gene Family.

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Recent evidence suggests that at least some kallikrein and kallikrein-like genes are implicated in breast, prostate and other human cancers. In our attempt to find new kallikrein-like genes, we cloned a novel kallikrein-like gene that maps to chromosome 19q13.3 - q13.4. Screening of ESTs allowed us to delineate its genomic organization and the exon/intron splice sites (GenBank Accession number AF135025). We tentatively named this gene KLK-L5 (for kallikrein-like gene 5). KLK-L5 has been defined as a kallikrein-like gene based on the significant similarity and close proximity to other members of the kallikrein multi-gene family. KLK-L5 is expressed in prostate, thymus, lung, testis, uterus, colon and thyroid gland. In order to investigate whether the KLK-L5 gene is under steroid hormone regulation, two breast cancer cell lines (BT-474 and T47D) and a prostate cancer cell line (LNCaP) were used as models. In LNCaP cells, the gene was up regulated only by androgen and progestin. In BT-474 cells, KLK-L5 was found to be up-regulated, at the mRNA level, by estrogen and androgen, and to a lesser extent by progestin. The rank of potency was estrogen > androgen > progestin. However, the rank of potency for the T47D cell line was androgen> progestin > estrogen. Steroid hormones are known to be associated with breast and prostate cancers. Based on information on other kallikrein genes that are localized in the same region (PSA, KLK2, zyme, neuropsin, and NES1), we speculate that this gene may also be involved in the pathogenesis and/or progression of breast, prostate and possibly other malignancies.