hree years, new putative members of the human kallikrein gene family have been dentified. Here, by using the positional candidate gene approach, we were able o identify a novel serine protease gene that maps to chromosome 19q13.3–q13.4, the location of the kallikrein gene family. Screening of expressed sequence ags (ESTs) allowed us to establish the expression of the gene and delineate its genomic organization. We tentatively named this gene KLK-L4 (for kallikrein-like gene 4, Genbank accession #AF135024). Using reverse-transcription polymerase chain reaction (RT-PCR), we amplified mRNA from various tissues and found that KLK-L4 was highly expressed in the testis, prostate, mammary and salivary glands, and moderately expressed in adrenal gland, pancreas, trachea, thymus, ung, colon and thyroid. We also found KLK-L4 expressed in the breast cancer cell line MCF-7. We examined the differential expression of KLK-L4 in a variety of malignancies; notably, KLK-L4 was found to be down-regulated in fifteen out of eighteen breast tumors. Finally, using the BT-474 breast cancer cell line as a model, we discovered KLK-L4 was moderately upregulated by estradiol, and strongly upregulated by dihydrotestosterone (DHT) and norgestrel, implicating the possibility that these ligands affect the expression of KLK-L4 in breast cancer. Our future studies will attempt to elucidate the biological function of KLK-L4 in breast and other tissues.

#4748 CLONING OF KLK-L5, A NEW MEMBER OF THE KALLIKREIN GENE FAMILY, AND ITS HORMONAL REGULATION IN BREAST CANCER CELL LINES. G. M Yousef, George Foussias, A. Magklara, L. Grass, and E. P Diamandis, *Mount Sinai Hosp, Toronto, On, Canada, and Univ of Toronto, Toronto, ON, Canada*

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, using the positional candidate gene approach, 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 # 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. KLK-L5 is upregulated by estrogens and progestins, and to a lesser extent by androgens, in the breast cancer cell line BT-474. 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.

#4749 DISCOVERY OF A NEW HUMAN KALLIKREIN-LIKE GENE, KLK-L4, AND THE STUDY OF ITS EXPRESSION IN BREAST CANCER. Albert Chang, G. M Yousef, and E. P Diamandis, *Mount Sinai Hosp, Toronto, On, Canada, and Univ ot Toronto, Toronto, On, Canada*

The human kallikrein gene family is comprised of genes that have established or potential applications in prostate and breast cancer diagnostics. For the past