#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 of 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 three years, new putative members of the human kallikrein gene family have been identified. Here, by using the positional candidate gene approach, we were able to 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 tags (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, lung, 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.