HUMAN GLANDULAR KALLIKREIN (HK2) AND PROSTATE SPECIFIC ANTIGEN (PSA) IN PROSTATE AND BREAST CANCER. Angeliki Magkira, A. Scorilas, W. J Catalona, and E. P Diamandis, Mount Sinai Hosp, Toronto, ON, Canada, Univ of Toronto, Toronto, ON, Canada, and Washington Univ Sch of Medicine, St. Louis, MO

Human glandular kallikrein (hk2) is a serine protease that shares many biochemical and structural properties with prostate specific antigen (PSA). Recent studies indicate that hk2 may be a novel marker for prostate cancer, supplementing the well established clinical value of PSA and that both kallikreins may play an important role in the physiology of normal and malignant breast tissue. We analyzed 210 serum samples from men with histologically confirmed BPH or CaP with total PSA in the "grey zone" (4-10 ug/l). Statistical analysis showed that the hk2/free PSA ratio (AUC=0.69, p<0.0001) was stronger predictor of CaP than the free/total PSA ratio (AUC=0.64, p<0.001). At the level of 95% specificity, the hk2/free PSA ratio identified 30% of patients who had cancer. Our data suggest that hk2 in combination with free and total PSA can enhance the biochemical detection of prostate cancer in patients with moderately elevated total PSA levels. We also investigated the steroid hormone regulation of hk2 and PSA in several breast cancer cell lines, BT-474 cells produce more hk2 than PSA, whereas the situation is reversed in T-47D cells. From all steroids tested, mibolerone was the most potent stimulator for both kallikreins followed by norgestrel. MFM-223, an androgen responsive cell line devoid of other steroid hormone receptors, was also capable of producing hk2 and PSA but at much lower amounts. MCF-7, ZR-75-1, MDA-MB-435 and BT-20 cell lines failed to produce any protein. Our data suggest that the expression of the hk2 gene in breast cancer cell lines is mainly under the control of androgens and progestins, similarly to PSA. These cell lines could be an important tool in the investigation of the molecular mechanisms that control the expression of the hk2 and PSA genes in-vitro and in vivo facilitating a better understanding of the pathophysiology of steroid hormone-dependent breast tumors.