PROSTATE SPECIFIC ANTIGEN (PSA) AND HUMAN GLANDULAR KALLIKREIN 2 (HK2): TWO HORMONALLY REGULATED KALLIKREINS WITH APPLICATIONS IN BREAST AND PROSTATE CANCER

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Mounting evidence suggests that prostate specific antigen (PSA), a steroid hormone regulated kallikrein, may have a significant effect on the pathophysiology of malignant breast tissue, and so could human glandular kallikrein 2 (hK2). The establishment of breast cancer cell lines, which are able to produce sufficient amounts of these proteins, would be an important ol in the investigation of the molecular mechanisms that control the expression of these genes in-vitro and in-vivo. The BT-474 and T-47D are two steroid receptor-positive cell lines, that produce large amounts of PSA and hK2 upon induction with androgens and progestins. However, significant differences in the levels of the two kallikreins produced by these cell lines indicate that there is a different mode of gene regulation involved. 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. Recent studies indicate that hK2 may be a novel marker for prostate cancer, supplementing the well established clinical value of PSA. To confirm that we analyzed 210 serum samples from men with histologically confirmed BPH or CaP with total PSA in the "grey zone" (4-10 ug/L). ROC analysis showed that the hK2/free PSA ratio was stronger edictor of CaP than the free/total PSA ratio. We also found that patients with increased hK2/free PSA ratio and total PSA <4.5 µg/L are at a significantly increased risk of having prostate cancer.