

#1700 Mutations in the regulatory region of the prostate specific antigen gene from breast tumors and cell lines. Majumdar, S. and Diamandis, E.P. *Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Canada M5G 1X5.*

Prostate specific antigen (PSA) is a serine protease which is an established tumor marker of prostate adenocarcinoma, used for the diagnosis and monitoring of patients with prostate cancer. PSA originally identified in prostatic epithelium has now been demonstrated to be expressed in about 70% of breast tumors. The wild type PSA gene is under regulation by steroid hormones. In this study we examine the molecular mechanisms underlying the expression of the PSA gene in breast cancer and breast cancer cell lines. We analyzed ten breast tumors categorized on the basis of high or low PSA expression in tumor cytosols and four breast cancer cell lines. To determine abnormalities associated with PSA expression in breast tumors, genomic DNA was extracted and all five exons of the PSA gene were PCR amplified and sequenced on both strands. PCR amplification was also performed for the promoter and enhancer elements of the gene. No mutations were observed in the coding portion of the gene. A polymorphism was observed in exon 2 from three breast tumors. However, sequencing of the promoter and the enhancer elements of the PSA gene reveals several point mutations and insertions in the promoter and enhancer element of the PSA gene. Most importantly, the androgen response element (ARE I) in the promoter is mutated in four tumors and in the breast carcinoma cell line MCF-7. Mutations associated with the ARE I have been shown previously to result in 80% decrease in PSA gene expression. The mutations in the core enhancer and promoter region may likely contribute to the aberrant expression of the PSA gene in breast tumors, by possibly altering structure and function of the gene.

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