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CHARACTERIZATION OF ANDROGEN-DEPENDENT PROSTATE SPECIFIC ANTIGEN (PSA) SECRETION IN ANDROGEN RECEPTOR-TRANSFECTED HUMAN PROSTATE CANCER PC-3 CELLS

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Prostate-specific antigen (PSA) is an androgen-regulated serine protease produced by prostate epithelial cells, including prostate cancer cells. Serum PSA levels are commonly used as a screening tool for prostate cancer detection and to track the progression of the disease. Androgen independent human prostate cancer PC-3 cells lack androgen receptor (AR) expression and do not produce PSA. We have previously demonstrated paradoxical androgen-dependent cell cycle arrest in PC-3 cells stably transfected with a full-length human AR cDNA. In the present study we examined the ability of dihydrotestosterone (DHT) to stimulate PSA production in these cells. Four PC-3 AR-transfected clones expressing different levels of AR as determined by [³H]R1881 ligand binding assays, were examined. PC-3 cells transfected with the expression vector lacking AR cDNA insert (mock transfected, PC-3(M) cells) were used as controls. PSA was measured in the culture medium using an ELISA-based immunofluorometric assay. All AR-transfected clones tested produced and secreted PSA in response to DHT treatment in a dose- and time-dependent manner, with the concentrations of PSA measured correlating with the levels of AR binding measured in the cells. PSA was not detected in the absence of DHT treatment nor in PC-3(M) cells. Testosterone and R1881 similarly stimulated PSA secretion, whereas progesterone, dexamethasone, and estradiol-17B had no effect, indicating androgen specificity. Furthermore, hydroxyflutamide and bicalutamide inhibited DHT-induced PSA secretion in a dose-dependent manner. These findings demonstrate a typical androgen response in the PC-3 AR-transfected cells and demonstrate that PC-3 cells have retained the ability to produce and secrete PSA. The loss of PSA production in the parental cell line is thus due to the lack of AR expression. These studies further suggest the utility of PC-3 AR-transfected cells to evaluate androgenic activity of putative endocrine disrupters using PSA as an endogenous reporter system.