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Androgen-Induced Prostate-Specific Antigen Gene Expression Is Mediated via Dihydrotestosterone in LNCaP Cells

YUAN-SHAN ZHU, LI-QUN CAI, XUEKE YOU, JUAN J. CORDERO, YING HUANG AND JULIANNE IMPERATO-MCGINLEY

From the Department of Medicine/Endocrinology, Weill Medical College of Cornell University, New York, New York.

Correspondence to: Dr Yuan-Shan Zhu, Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Weill Medical College of Cornell University, 1300 York Ave, Box 149, Room F-233, New York, NY 10021 (e-mail: yuz2002{at}med.cornell.edu).

Prostate cancer is a leading cause of cancer death in American males. Androgens play an essential role in prostate development, growth and pathogenesis of benign prostate hyperplasia, and prostate cancer. Although testosterone is the main androgen secreted from the testes, dihydrotestosterone (DHT), a more potent androgen converted from testosterone by 5α-reductase isozymes, type 1 and 2, is the major androgen in the prostate cells. Thus, 5α-reductase(s) are critical in determining androgen activity in the prostate. However, it is unclear in prostate tumor cells whether 1 or 2 5α-reductase isozymes are expressed and whether they are functionally important. In the present report, we studied the importance of 5α-reductase isozymes in the androgen induction of prostate-specific antigen (PSA) gene expression in LNCaP prostatic tumor cells. Treatment with either testosterone or DHT in LNCaP cells produced dose- and time-dependent increases in PSA levels in the cell media and in PSA messenger RNA (mRNA) levels in the cells. However, testosterone-induced but not DHT-induced PSA gene expression was significantly inhibited by finasteride, a 5α-reductase inhibitor, in a dose-dependent manner. Furthermore, we demonstrated for the first time that both 5α-reductase-1 and 5α-reductase-2 mRNAs were expressed in LNCaP cells using reverse transcriptase-polymerase chain reaction (RT-PCR) and RT-PCR Southern blot analysis. These results suggest that both 5α-reductase isozymes are present and functionally important in prostatic tumor LNCaP cells and that DHT is a major mediator of androgen induction of PSA gene expression in these cells.

Key words: 5α-Reductase isozymes, testosterone, prostatic tumor cells

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[Abstract] [Full Text] [PDF]

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