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Gene Expression in Prostate Cancer Cells Treated With the Dual 5 Alpha-Reductase Inhibitor Dutasteride

LUCY J. SCHMIDT*, HORACIO MURILLO*,† AND DONALD J. TINDALL*,‡

*From the * Departments of Urology Research, † Molecular Pharmacology and Experimental Therapeutics, and ‡ Biochemistry and Molecular Biology, Mayo Clinic College of Medicine, Mayo Clinic, Rochester, Minnesota.*

Correspondence to: Dr Donald J Tindall, Department of Urology Research, Mayo Clinic College of Medicine, Mayo Clinic, Rochester, MN 55905 (e-mail: tindall {at}mayo.edu).

We sought preclinical data on the cellular and molecular effects of dutasteride in androgen-responsive, human prostate cancer (PCa) cells to better understand the mechanisms of action of 5 alpha-reductase inhibition in these cells. We used the human prostate cancer cell line LNCaP, which exhibits most features of PCa cells including androgen responsiveness. Our findings show that dutasteride kills PCa cells in vitro; it dramatically reduced viability and proliferation and disrupted genes and cellular pathways involved in metabolic, cell cycle, and apoptotic responses besides those expected in androgen-signaling pathways. Microchip gene array expression analysis revealed activation of genes in the FasL/tumor necrosis factor alpha (TNF-α) apoptotic and cell-survival pathways, correlating with the growth and survival effects in the LNCaP cells. Real-time polymerase chain reaction confirmed expression level changes seen by microarray analysis of candidate genes such as PLA2G2A, CDK8, CASP7, MDK, and NKX3.1. Collectively, our findings delineate the cellular and molecular effects of dutasteride in androgen-responsive PCa cells in vitro and may lead to its better therapeutic and chemopreventive use in PCa.

Key words: LNCaP, gene-expression profiling, REDUCE trial, apoptosis