SOUTHWESTERN NEWS

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DEVELOPMENT OF PROSTATE DRUG BASED ON UT SOUTHWESTERN RESEARCH

DALLAS – June 24, 2003 – A new finding revealing that the drug finasteride reduces the risk of prostate cancer by nearly 25 percent represents the culmination of three decades of research that began in the early 1970s at UT Southwestern Medical Center.

A study released online today by *The New England Journal of Medicine* shows that finasteride, which is already proven effective as a therapy for benign prostatic hyperplasia (BPH) – or enlargement of the prostate – also delays or prevents prostate cancer and reduces the risk of urinary problems. However, the drug has significant sexual side effects and may increase the risk of high-grade prostate cancer in some patients, the study reports. The study will appear in the July 17 print edition of the journal.

Finasteride inhibits the conversion of testosterone to dihydrotestosterone by the enzyme 5-alpha reductase. By doing so, it reduces the level of dihydrotestosterone – the primary androgen in the prostate that is involved in the development of prostate cancer – by 90 percent.

"Dr. Jean Wilson discovered the importance of the enzyme 5-alpha reductase in prostate disease almost 30 years ago," said Dr. John McConnell, UT Southwestern's executive vice president for health system affairs and a urologist.

"Since this discovery, UT Southwestern investigators have clearly demonstrated the role of this enzyme in BPH. The exciting information in this new article is that it clearly also has an impact on prostate cancer," said Dr. McConnell, UT Southwestern's former chairman of urology and acting director of the Harold C. Simmons Comprehensive Cancer Center.

The findings released today are the result of the Prostate Cancer Prevention Trial, a 7-year study involving 9,457 men. UT Southwestern participated as a trial site in this study.

Prostate cancer is the second-leading cause of death from cancer in men in the United States, and the most common non-skin cancer in America. The American Cancer Society estimates that 220,900 new cases of prostate cancer will be diagnosed in the United States in 2003.

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The prostate is a walnut-sized gland just beneath the bladder that secretes one of the primary components of seminal fluid.

Dr. Wilson first envisioned the drug that became finasteride in the early 1970s. Dr. Wilson wrote a pivotal paper published in 1974 in *The New England Journal of Medicine*, in which he wrote that men with a rare genetic disorder – 5-alpha reductase deficiency – did not develop normal prostates or prostatic enlargement. He theorized at the time that reproducing this condition artificially may lead to nonsurgical treatment of an enlarged prostate. He later identified the genes that encode for 5-alpha reductase.

Dr. David Russell, a UT Southwestern professor of molecular genetics, cloned the 5-alpha reductase enzyme in the early 1990s and published his findings in *Nature.* He also hypothesized that 5-alpha reductase may play a role in preventing prostate cancer.

Building on this work, a Merck scientist developed finasteride, which is manufactured by Merck as Proscar. Dr. McConnell led a four-year clinical trial of the drug ending in 1998. The drug has shown to shrink the prostate by 20 percent to 30 percent and to significantly reduce the need for surgical intervention and the risk of acute urinary retention.

"The Prostate Cancer Prevention Trial is the culmination of several decades of work demonstrating the importance of the 5-alpha reductase enzymes and the genetic or medically induced absence thereof in the development and progression of not only BPH, but also prostate cancer," said Dr. Claus Roehrborn, UT Southwestern's chairman of urology.

"Several researchers at UT Southwestern have played pivotal roles in various phases of this work."

Dr. Roehrborn, who has been involved in the testing of Proscar, wrote a paper last fall about dutasteride, a drug developed by GlaxoSmithKline that is also designed to replicate the effects of 5-alpha reductase deficiency. Dutasteride is also used in the treatment of BPH, and GlaxoSmithKline is planning a prostate cancer prevention trial as well.

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