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ENZYME RESEARCH POINTS THE WAY TO NEW DRUGS FOR PROSTATE, BALDNESS

DALLAS--Recent discoveries by Dr. David W. Russell may speed the development of drugs for benign prostatic hyperplasia (BPH) and other disorders involving male hormones.

Russell is a professor of molecular genetics at The University of Texas Southwestern Medical Center at Dallas and holder of the Eugene McDermott Distinguished Chair in Molecular Genetics. Early in his research career at UT Southwestern, Russell concentrated on the molecular and genetic mechanisms of cholesterol metabolism, working closely with Nobel laureates Michael Brown and Joseph Goldstein. Recently, he shifted his attention to steroid 5-alpha reductase, an enzyme that converts the male hormone testosterone (a cholesterol byproduct) into the far more potent steroid dihydrotestosterone (DHT).

Dr. Jean D. Wilson, professor of internal medicine and holder of the Charles Cameron Sprague Distinguished Chair in Biomedical Science, discovered in the early '70s that DHT actually drives many of the processes ascribed to testosterone and that genetic defects in the 5-alpha reductase molecule result in underproduction of DHT. These defects cause a rare disorder in which the prostate and some other male organs fail to develop.

In 1990 Russell reported having isolated a human gene that encodes 5-alpha reductase. Last November in the British scientific journal Nature, he reported isolating a gene for a second form of 5-

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alpha reductase. This second form, designated type 2, is the major enzyme affecting the prostate gland.

Russell's work has implications for treatment of disorders linked to 5-alpha reductase. "For example, male-pattern baldness most likely involves the type 1 enzyme," he said. "To prevent it or arrest it, you want a drug that selectively inhibits type 1." The type 1 enzyme also appears to be related to adult acne and female hirsutism.

Russell's cloning of the type 2 gene may help speed development of the next generation of drugs for BPH. Finasteride (Proscar®), the first drug approved by the U.S. Food and Drug Administration for shrinking benign enlargement of the prostate, was a direct outgrowth of Wilson's trailblazing work in the '70s. Still better drugs are needed, however, since finasteride brings significant relief from symptoms for only one in three BPH sufferers.

"One of the problems in this field has been getting enough 5-alpha reductase to set up rapid screens for drugs," Russell said. "Having the pure gene allows you to make as much of either type as you need."

Russell, a Dallas native, is a 1975 graduate of The University of Texas at Austin. He received his doctoral degree in chemistry from the University of North Carolina in 1980. Russell has been a member of the faculty at UT Southwestern since 1982.

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NOTE: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences, Southwestern Allied Health Sciences School, affiliated teaching hospitals and outpatient clinics.