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## ANDROGEN RECEPTORS MAY OFFER CLUE TO PROSTATE CANCER PUZZLE

DALLAS--Ongoing research in the laboratory of Dr. Michael J. McPhaul may lead to better ways of predicting which prostate cancers will respond to hormonal therapy.

McPhaul is an assistant professor of internal medicine at The University of Texas Southwestern Medical Center at Dallas. His work focuses on the androgen receptor, a protein that binds two male hormones (androgens), testosterone and dihydrotestosterone, and affects their action in a variety of tissues, including prostate. In 1988 his laboratory was one of the first in the world to isolate and clone the androgen receptor.

The normal prostate grows in response to androgens and shrinks in the absence of these hormones. In like fashion, the growth of many prostate cancers is at least initially androgen-dependent and can be put into temporary remission by castration or administration of drugs that block the formation and action of androgens. But relapses are common, often as a result of androgen-independent tumor growth. This appears to be caused by a shift in the composition of the tumor from cells that need androgens to grow to those that do not. The mechanism of this shift is not known.

McPhaul has found that many prostate cancer cells capable of growing without androgens do not produce androgen receptors. Furthermore, in preliminary results of a retrospective study, he and his collaborators found that an absence of androgen receptors in biopsy

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samples from prostate cancer patients is associated with a higher incidence of tumor growth following hormone withdrawal. These findings suggest a link between androgen receptor expression and the biological behavior of individual tumors.

Current studies are designed to pursue these leads at both clinical and basic-science levels. Clinical studies are being conducted to determine whether androgen receptor measurements in patients with newly-diagnosed prostate cancer can help predict the subsequent course of the cancer.

At the basic-science level, McPhaul is attempting to define factors determining whether tumor cells produce androgen receptors and to understand how androgens and androgen receptors interact to alter cell growth.

McPhaul is a 1977 graduate of The University of Texas at Austin. He received his medical degree from Southwestern Medical School in 1981 and served his internship and residency at Parkland Memorial Hospital. In 1983 he began a three-year Helen Hay Whitney Research Fellowship in the laboratory of biochemist Paul Berg at Stanford University Medical Center. McPhaul joined the UT Southwestern faculty in 1986 in the Division of Endocrinology and Metabolism of the Department of Internal Medicine. In 1988, he received a Charles E. Culpepper Foundation Scholarship, given to support a young academic physician of high potential achievement.

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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.