



Uniformed Services University
of the Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814-4799

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Contact: Office of External Affairs
Voice: 301-295-1219 Fax: 301-295-3757
Email: anicholson@usuhs.mil

News Release

USU Researchers Unravel New Aspects of the Male Hormone (Androgen) Receptor Regulation in Prostate Cancer

BETHESDA, Md. — A team of researchers in the Center for Prostate Disease Research (CPDR) at the Uniformed Services University of the Health Sciences (USU), led by Dr. Shiv Srivastava, professor of surgery, are working to define male hormone regulated transcriptome in prostate cancer cells.

Male hormone signaling mediated by the androgen receptor (AR) plays a central role in the normal growth and development of the prostate gland. Increasing evidence suggests that AR pathway defects contribute to the prostate cancer progression. Therefore, inhibition of the AR pathway remains the main target for systemic therapy of prostate cancer. However, the emergence of the treatment resistant disease is a major challenge and considerable research is being devoted to understand defects of the hormonal pathways in prostate cancer and refractory mechanisms to hormonal therapy. The CPDR group strives to delineate key components of the AR regulated gene network that are altered during prostate cancer onset and/or progression.

The ground-breaking data generated by the CPDR team have now led to the discovery of a completely new mechanism of regulation of AR by the NEDD4 binding protein - PMEPA1, which was earlier discovered by this group as a prostate abundant and androgen regulated gene. Dr. Hongyun Li, scientist, CPDR; Dr. Albert Dobi, assistant professor of surgery, USU; and colleagues found that PMEPA1 as a NEDD4 binding protein can induce the degradation of the AR in prostate cancer cells. This data indicates that decreased or loss of expression of PMEPA1, which is associated with two thirds of prostate cancers, may result in elevated AR in tumor cells which in turn may exacerbate increased growth of tumor cells. While other mechanisms of AR turnover are known, the finding of PMEPA1 induced AR turnover is new and quite fascinating. These findings were published in the *Journal of Biological Chemistry*, Aug. 14, 2008.

There appears to be a tight negative feed-back loop between PMEPA1 and AR. PMEPA1 itself is regulated by the AR, so it is likely that PMEPA1 regulates AR in male hormone dependent cells. Future studies are being address to assess the role of PMEPA1 in maintaining AR levels in the normal prostate as well as in malignant prostate growth.

Learning to Care for Those in Harm's Way

The Uniformed Services University is located on the grounds of Bethesda's National Naval Medical Center and across from the National Institutes of Health. It is the nation's federal school of medicine and graduate school of nursing. The university educates health care professionals dedicated to career service in the Department of Defense and the U.S. Public Health Service.

Students are active-duty uniformed officers in the Army, Navy, Air Force and Public Health Service who are being educated to deal with wartime casualties, natural disasters, emerging infectious diseases, and other public health emergencies. Of the university's more than 4,200 physician alumni, the vast majority serve on active duty and are supporting operations in Iraq, Afghanistan, and elsewhere, offering their leadership and expertise.

For more information, contact the Office of External Affairs at 301-295-1219.

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