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News Release

USU Researchers Provide New Insights Into Common Alterations of *ERG* Oncogene in Prostate Cancer

BETHESDA, Md. — In the past three years, ground-breaking discoveries in the prostate cancer field have highlighted that alterations of *ETS* related genes (predominantly *ERG*), as a result of a fusion between male hormone receptor regulated gene promoters (predominantly *TMPRSS2*) and *ETS* transcription factors, represent one of the most common oncogenic defects in prostate cancer. Researchers at the Center for Prostate Disease Research (CPDR) at the Uniformed Services University of the Health Sciences (USU) had originally shown frequent overexpression (60-70%) of the *ETS* related gene *ERG* in the epithelial cell transcriptome of prostate cancers. In their continued quest to understand the functional role and clinical utility of *ERG* alterations in prostate cancer, CPDR researchers have now defined new features of *ERG* function and expression which will further enhance the potential of *ERG* as promising biomarker and therapeutic target for prostate cancer.

Using cell culture and animal models and prostate cancer specimens from patients, the multi-disciplinary group co-led by Dr. Shiv Srivastava, Dr. David G. McLeod, Dr. Isabell A. Sesterhenn and Dr. Albert Dobi shows that inhibiting *ERG* expression in prostate tumor cells induces markers of prostate differentiation and inhibits tumor cell growth in mice. This study also highlights the role of the *C-MYC* oncogene in mediating *ERG* functions in prostate cancer cells. Taken together, these novel findings strongly implicate causal roles of *ERG* in prostate cancer at least in part by affecting cellular differentiation. Moreover, this study underscores promising potential of *ERG* and *C-MYC* in developing new targeted therapy for a large percentage of prostate cancers with *ERG* overexpression (60-70%).

The second innovative CPDR study, co-led by Dr. Shiv Srivastava, Dr. David G. McLeod, Dr. Isabell A. Sesterhenn and Dr. Gyorgy Petrovics, defines full length transcripts and proteins encoded by common *TMPRSS2-ERG* fusions in prostate tumors. This study for the first time has led to the discovery of two major types of *ERG* products (type I: full length and type II: without *ETS* domain) in prostate tumors. Surprisingly, they found an abundance of type II products in tumors cells. Although the functional role of the type II products is unclear, early data suggest that ratios of type I and type II products in prostate tumor cells may provide prognostic indicators for disease progression. New information from this study has promise to enhance future strategies for utilizing specific *ERG* products as biomarkers or as therapeutic targets. Further studies are also warranted that would address the role of specific *ERG* products in overall *ERG* functions in prostate cancer. Towards these goals the CPDR team has been recently awarded a three year grant from the DoD-Prostate Cancer Research Program.

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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