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New research uncovers promising new biomarker for aggressiveness of prostate cancer, implications for treatment

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Research out of Roswell Park Cancer Institute (RPCI) supports the adoption of a new biomarker to measure the aggressiveness of primary prostate tumors. A team of investigators from three institutions, led by Shahriar Koochekpour, MD, PhD, Associate Professor of Cancer Genetics, Urology and Oncology in RPCI's Department of Cancer Genetics, has for the first time produced data showing that levels of serum glutamate, a naturally occurring nonessential amino acid that plays a key role in cancer metabolism, are increased in patients with primary and metastatic prostate cancer.

Collaborators included James L. Mohler, MD, Gissou Azabdaftari, MD, and Kristopher Attwood, PhD, from RPCI; Robert L. Vessella, PhD, from the University of Washington School of Medicine; and Oliver Sartor, MD, from Tulane Cancer Center and the Tulane University School of Medicine. In a study involving 366 men, the team measured serum glutamate levels in 60 healthy adult males, 197 with primary prostate cancer and 109 with metastatic castration-resistant prostate cancer—cancer that progresses following androgen depletion therapy.

"Comparing normal, primary and metastatic prostate cancer tissues, we discovered that glutamate receptor is expressed at very high levels in primary and metastatic tumors, but at very weak or undetectable levels in benign prostate tissues," notes Dr. Koochekpour. "And serum glutamate was detected at increased levels proportional to Gleason score, the

standard index for rating prostate cancer aggressiveness and prognosis in patients with primary tumors."

The researchers also demonstrated, for the first time, that glutamate deprivation significantly decreases the growth, migration and invasiveness of prostate cancer cell lines, suggesting potential clinical applications. They also report that the glutamate antagonist riluzole (Rilutek), a well-tolerated oral medicine used for mood and anxiety disorders, depression and amyotrophic lateral sclerosis (ALS), induces cell death while inhibiting the progression and motility of human prostate cancer cells.

"We detected one major difference between African-Americans and Caucasians in the study," Dr. Koochekpour notes. "In African-Americans, serum glutamate levels were higher among those men with metastatic disease than in those with primary prostate cancer, and we didn't see that trend in Caucasian men. This finding may implicate a role for glutamate metabolism in inter-racial disparities of prostate cancer."

Dr. Koochekpour and colleagues are currently conducting a preclinical study assessing the effectiveness of riluzole in preventing growth of human prostate cancer cells in animal models, and hope to build on these results in the clinical setting within the next 12-18 months. The paper, "Serum Glutamate Levels Correlate with Gleason Score and Glutamate Blockade Decreases Proliferation, Migration, and Invasion and Induces Apoptosis in Prostate Cancer Cells," was published October 16 in *Clinical Cancer Research* and can be accessed at clincancerres.aacrjournals.org … 078-0432.CCR-12-1308.

Provided by Roswell Park Cancer Institute

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