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Compound Can Distinguish Between Benign, Localized and Metastatic Prostate Cancer

Researchers have determined that a molecule produced by the body's metabolism could be used to differentiate between benign prostate tissue vs. localized and metastatic prostate cancer. They also found that this molecule, known as sarcosine, may be associated with prostate cancer invasiveness and aggressiveness. The findings were reported by researchers at the Michigan Center for Translational Pathology, Ann Arbor, and were supported by the National Cancer Institute's (NCI) Early Detection Research Network (EDRN). The research appears in the Feb. 12, 2009 issue of Nature. NCI is part of the National Institutes of Health.

"Current biomarkers for detection or progression of prostate cancer are not as precise as we would like. Therefore, a more accurate indicator of cancer is of great interest," said Sudhir Srivastava, Ph.D., chief of NCI's Cancer Biomarkers Research Group. "Sarcosine and some other select metabolites may be excellent indicators of cancer progression."

Multiple, complex molecular events characterize cancer development and progression. Determining which molecular networks dictate whether cancer will be confined to the prostate or spread to other parts of the body could lead to the identification of critical biomarkers associated with prostate cancer invasion and aggressiveness.

Although many genes and proteins related to cancer have been extensively characterized by genomic and proteomic studies, little is known about metabolomic changes that mark a

tumor's progression. Metabolomics, upon which this current finding is based, is the study of the unique chemical fingerprints that cellular processes leave behind, which can help scientists understand the makeup of a cell. One of the challenges that scientists currently face is integrating genomic, proteomic, and metabolomic information to give a more complete picture of living organisms and the diseases that afflict them.

Using a long-established laboratory technique called mass spectrometry, which sorts chemical compounds by their molecular weight, the researchers profiled more than 1126 metabolites from 262 clinical samples related to prostate cancer (42 tissue samples, 110 urine samples and 110 samples of blood plasma). These metabolomic profiles enabled researchers to distinguish between benign prostate tissue, clinically localized prostate cancer, and metastatic disease. Sixty metabolites were identified in localized and/or metastatic prostate tumors that were not present in benign prostate tissue. Ultimately, six metabolites, including sarcosine, were found to be significantly elevated during progression from benign tissue to localized cancer to metastatic disease. Sarcosine was also detected in the urine of men with prostate cancer. Because this metabolite showed progressive elevation from benign tissue to localized prostate cancer to metastatic disease, it was selected for further study.

To investigate the role of sarcosine in prostate cancer progression, the researchers performed analyses of laboratory-grown cells. They found that sarcosine levels were higher in invasive prostate cancer cells than in benign prostate cells. Moreover, the addition of sarcosine to benign prostate cells caused them to become invasive. By manipulating levels of the enzymes that regulate sarcosine metabolism, the researchers found they were able to control the invasiveness of benign and malignant prostate cells.

"Components of the sarcosine pathway could serve as novel avenues for therapeutic intervention," said Arul M. Chinnaiyan, M.D., Ph.D., Michigan Center for Translational Pathology at the University of Michigan, Ann Arbor. "Our next step will be to confirm these findings in a greater number of specimens and to have our results validated by other laboratories."

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Sreekumar A, Poisson LM, Rajendiran TM, Khan AP, Cao Q, Yu J, Laxman B, Mehra R, Lonigro RJ, Yong L, Nyati MK, Ahsan A, Kalyana-Sundaram S, Han B, Cao X, Byun J, Omenn

GS, Ghosh D, Pennathur S, Alexander DC, Berger A, Shuster JR, Wei JT, Varambally S, Beecher C, and Chinnaiyan AM. Metabolomic profiles delineate potential role for sarcosine in prostate cancer progression. *Nature.* February 12, 2009.

For more information on Dr. Chinnaiyan's research, please go to http://mctp.path.med.umich.edu/mctp/main/index.jsp.

For more information on NCI's EDRN, please go to: http://edrn.nci.nih.gov.

NCI leads the National Cancer Program and the NIH effort to dramatically reduce the burden of cancer and improve the lives of cancer patients and their families, through research into prevention and cancer biology, the development of new interventions, and the training and mentoring of new researchers. For more information about cancer, please visit the NCI Web site at http://www.cancer.gov or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

The University of Michigan Health System includes three hospitals, approximately 40 health centers and 120 outpatient clinics, the University of Michigan Medical School and its Faculty Group Practice, the University of Michigan School of Nursing and the Michigan Health Corp. People come from around the world seeking care, resulting in 1.6 million outpatient visits, more than 43,000 admissions, 75,000 ER visits and 64,600 surgical cases annually. UMHS is ranked among the top medical institutions and medical schools in the United States every year. For more information about UMHS and its services, visit www.med.umich.edu.