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Wistar-Led Research Team Discovers Genetic Pattern That Indicates Early-Stage Lung Cancer

PHILADELPHIA – (December 1, 2009) – Wistar Institute researchers and collaborators from the University of Pennsylvania and New York University have identified immune system markers in the blood which indicate early-stage lung tumors in people at high risk for developing lung cancer. The findings, published online December 1 in *Cancer Research*, a journal of the American Association for Cancer Research, could lead to a simple blood test to detect lung cancer in its earliest phases, when it can be most successfully treated.

Wistar investigators Louise C. Showe, Ph.D., and Michael K. Showe Ph.D., and colleagues examined gene expression profiles in blood samples from more than 200 patients with lung cancer or other, non-malignant, lung diseases. Focusing on non-small cell lung cancer (NSCLC), and the large at-risk population of smokers and ex-smokers, the researchers sought to determine whether lung tumors—even at the earliest stages—leave a gene expression signature in circulating blood cells. Recent studies have shown that in some late-stage cancers, an immune system response can be detected in the blood which can contain information on responsiveness to therapy or identify markers associated with prognosis.

For the study, peripheral blood was drawn from lung disease patients at the University of Pennsylvania Medical Center (Penn) and the New York University School of Medicine from 2003 through 2007, and the gene expression patterns in the samples were analyzed at Wistar. The team was able to identify a 29-gene “signature” that separated 137 patients with NSCLC tumors from 91 patient controls with non-malignant lung conditions, with 86 percent accuracy. Immune cells, which normally function to fight tumors, showed certain changes in the patients with malignant tumors that distinguished them from those of patients with other lung diseases such as chronic obstructive pulmonary disease or emphysema and patients with benign lung nodules.

When 18 NSCLC patients had peripheral blood drawn before surgery and again two to five months after their tumors were surgically removed, 13 of the samples showed a decrease in or complete disappearance of the tumor gene signature present in the pre-surgery samples after tumor removal. This finding demonstrates that the tumor presence can be communicated to the peripheral immune system and this signal can be detected in the gene expression patterns in peripheral blood.

Lung cancer is the most commonly occurring cancer in both men and women in the United States, accounting for 162,000 deaths in 2008, more than any other cancer. Early diagnosis followed by surgery presently is the most effective treatment for NSCLC, which accounts for 75 percent of lung tumors. Detecting cancer at its earliest stages would greatly improve the likelihood of survival; however, no simple and accurate

screening test such as mammography for breast cancer or colonoscopy for colon cancer exists for lung cancer. In addition, early-stage lung cancers show few symptoms and tend to spread rapidly before they are found.

With further study, the findings may serve as the basis for developing a simpler screening test for lung cancer. “People routinely get blood taken at their doctor’s offices, for cholesterol levels, diabetes, and other standard tests, so why not utilize this method to screen for other conditions such as the risk of developing lung cancer?” says Louise Showe, a professor in Wistar’s Molecular and Cellular Oncology and Immunology programs and director of its genomics facility. “Such a test could be especially useful for remote areas where typically technologies that are used in urban centers are not available. In addition, this test could be useful in a clinical setting to help to decide whether a small tumor detected on an x-ray is likely to be malignant.”

The team is working to develop a simpler method for collecting and processing blood samples for analysis. In addition, the clinical collaborators are gathering follow-up data from patients which will be used to analyze the data for signatures of recurrence and/or response to therapy. The researchers are also conducting additional analyses to further explore the basis for the changes in the peripheral immune system after tumor removal.

The lead author on the Cancer Research publication is Michael K. Showe, Ph.D. Other researchers involved in the study from The Wistar Institute include Andrew V. Kossenkov, Ph.D.; Elena V. Nikonova, M.D.; Celia Chang, Ph.D.; Calen Nichols and David A. Speicher, Ph.D. Collaborators from the University of Pennsylvania School of Medicine include Steven M. Albelda, M.D.; Anil Vachani, M.D.; John Kucharczuk, M.D.; Bao Tran and Elliot Wakeam and from the New York University School of Medicine William N. Rom, M.D., M.P.H.; and Ting an Yie, M.S.

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