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A tNOX-based Protocol for Early Detection of Lung Cancer in Smokers and Non-Smokers

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CHICAGO -- Lung cancer is a formidable disease. While it is one of the most preventable cancers, with the vast majority of 160,000 annual deaths in the United States due to smoking, it is invariably difficult to find early when it is most amenable to treatment. As a result, it remains the top cancer killer in the nation.

But a new test for the early detection of lung cancer that involves measuring levels of a certain protein may provide hope for thousands of smokers worldwide. While the findings are preliminary and involve a small group of subjects, the researchers see their early results as extremely promising.

Results were presented at the first meeting on Molecular Diagnostics in Cancer Therapeutic Development, organized by the American Association for Cancer Research.

A team led by Dorothy M. Morre, Ph.D., professor of foods and nutrition at Purdue University in West Lafayette, Indiana, and D. James Morre, Ph.D., distinguished professor of medicinal chemistry at Purdue, wanted to come up with a robust lung cancer screening procedure for people who smoke.

“We’d like to have a means of detecting lung cancer early in individuals who smoke with a low incidence of false positives,” Dorothy Morre said. “There’s apparently no good method of finding this and there is a lot of interest at the National Cancer Institute in developing such a protocol.”

The Morres -- along with colleagues at Purdue, NOX Technologies, Inc., also in West Lafayette, and at Mount Sinai Medical Center in New York -- focused their efforts on a protein called tNOX, a member of a family of proteins that are involved in cell growth. Normal cells express the NOX enzyme only when they are dividing in response to growth hormone signals. In contrast, cancer cells have gained the ability to express NOX activity at all times. This overactive form of NOX, known as tNOX – for tumor-associated NOX – has long been assumed to be vital for the growth of cancer cells, because drugs that inhibit tNOX activity also block tumor cell growth in culture.

The researchers compared four different protocols to determine levels of tNOX in the blood of 421 volunteer subjects, including 104 patients with lung cancer, 175 smokers who had not been diagnosed with lung cancer, 117 randomly selected outpatients and 25 healthy individuals.

Two of the protocols used rapid high-throughput screening techniques and gave a low incidence of false-positive diagnoses of lung cancer. In contrast, the researchers employed a technique using two different antibodies that they created against the tNOX protein, which they found gave a definitive indication of lung cancer.

“In healthy individuals, we have 0 out of 25 false positives,” noted D. James Morre. “In lung cancers, 103 of the 104 patients were positive for tNOX. In smokers older than 40 years of age, 12 percent were positive, which is about the normal incidence picked up with high resolution tomography.”

The researchers envision the tNOX test as serving as a screening tool for the early detection of lung cancer. Those who test positive would then be followed up with a medical examination and further tests, ostensibly including high resolution CT.

According to D. James Morre, current approaches to diagnosing lung cancer are costly and time consuming. “Our findings would provide a simple blood test that would indicate whether or not additional testing would be required,” he said. “We could screen very large smoker populations and eliminate perhaps 90 percent of them, while encouraging the other 10 percent to go on to the next stage of testing.

“This test is structured with the antibody we’re using to be specific for lung cancer in one form or another,” Dorothy Morre added. “It’s a specific diagnosis and it also distinguishes between non-small and small cell lung cancer.”

The scientists are already doing similar studies in colon, ovarian, prostate and breast cancers as well. They are planning three collaborative studies in which they will correlate tNOX antibody test results with medical evidence such as high resolution CT, physician examinations of patients – standard procedures for detecting early stage lung cancer.