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## Genetic Testing May Identify Therapeutic Targets in Premalignant Phase of Lung Cancer

**Roxanne Nelson**

November 26, 2007 — Gene expression biomarkers that distinguish smokers with lung cancer from smokers without the disease might aid not only in the early detection of lung cancer but also in reversing the progression of premalignancy to invasive cancer. The findings of the study, which were presented at the Chemotherapy Foundation Symposium XXV, in New York City, suggest that gene expression in normal-airway epithelial cells can serve as a lung cancer biomarker, which might lead to a reduction in mortality by allowing for improvements in diagnosis and therapeutic options.

"Personalized genomic medicine is the way of the future and is coming," said lead author Avrum Spira, MD, an assistant professor of medicine, pathology, and laboratory medicine at Boston University, in Massachusetts. "We are going to diagnose and treat people based on their particular genetic makeup. We're not there yet, but this will be available within the next few years."

In an interview with *Medscape Oncology*, Dr. Spira explained that the current data build on their previous research, which first identified an 80-gene biomarker that was able to distinguish smokers with lung cancer from those without it.

"The test can identify smokers with lung cancer and, more important, can identify smokers who have early-stage disease," he said. "Obviously, early diagnosis means a potential for cure with surgery. Five-year survival is dismal, and a large part of that is because we usually are unable to diagnose lung cancer at an early stage."

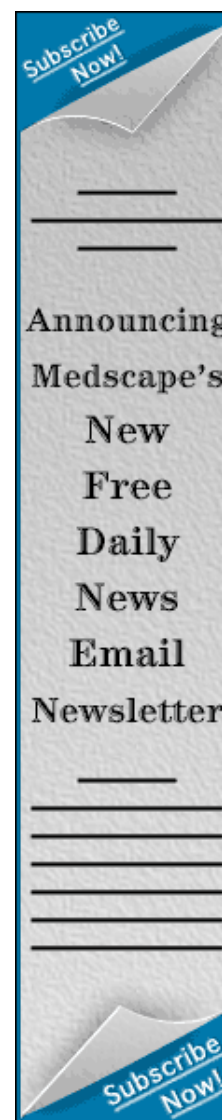
In a previous study, which was published in the March issue of *Nature Medicine* (2007;13:361-366), Dr. Spira and his coinvestigator, Jerome Brody, MD, director of the pulmonary center at Boston University, obtained histologically normal large-airway epithelial cells during bronchoscopy from 192 smokers suspected of having lung cancer. Using gene-expression profiles from Affymetrix HG-U133A microarrays, they were able to identify an 80-gene biomarker that distinguished smokers with lung cancer from those without the disease. The biomarker showed an approximate 90% sensitivity for stage 1 cancer across all patients and, in combination with cytopathology of lower-airway cells that were obtained during bronchoscopy with the biomarker, yielded 95% sensitivity

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and a 95% negative predictive value.

"What we've found since that paper, but have not yet published, is that the same cells in the airway can tell you not only whether you have lung cancer but also what oncogenic pathways have been altered in the cells by smoking," explained Dr. Spira, "and this information could guide what drugs you may want to use to reverse that damage."

In addition to diagnosis, the data might be able to identify which therapies are useful in patients who already have lung cancer. "But more important, it may help us determine which people may eventually develop lung cancer, and we may be able to reverse the process using chemoprophylaxis drugs that are currently being tested," said Dr. Spira.

At the current time, no drugs have been approved for lung cancer prevention, although a number of compounds are in development and in various stages of clinical trials, both in the United States and around the world. Dr. Spira believes that part of the reason for this is that not everybody responds to the same drug.

"Drug A may work for people who have activation of a particular oncogenic pathway that drug A interferes with, and having this molecular information on a particular patient allows us to guide which chemoprophylactic agent would be most appropriate," he said. "We're thinking that our approach would allow those chemoprevention clinical trials to show efficacy by tailoring treatment to an individual's molecular profile."

"The diagnostic data are very solid and have been published, whereas our therapeutic angle is relatively new but promising," Dr. Spira said. "It is more preliminary — we don't have as many samples or results — but it is moving quickly in a very exciting direction."

Chemotherapy Foundation Symposium XXV. Presented November 9, 2007.

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