MedicalXpress

New technique detects specific chromosomal damage, may indicate lung cancer risk

August 31 2007

A new technique could pave the way toward screening people at risk for lung cancer for the genetic changes that may foreshadow malignancies, researchers from the University of Colorado say.

“The most successful way to reduce mortality in cancer is prevention,” said researcher Wilbur A. Franklin, M.D., Professor of Pathology at the University of Colorado Health Sciences Center. “Our goal would be to develop screening techniques for lung lesions that could enable us to identify precancerous changes.”

The study appears in the September 1, 2007 issue of the *American Journal of Respiratory and Critical Care Medicine*, published by the American Thoracic Society.

Lung cancer is the leading cause of cancer deaths in the U.S., and kills more people than the next three most common cancers—colon, breast and prostate—combined. While it is well-established that smoking is the primary risk factor for lung cancer, a number of lung cancer patients have never smoked. Additionally, quitting smoking only gradually reduces the risk of lung cancer because much of the genetic damage done by tobacco is irreversible.

Recent research suggests that the genetic changes that accompany lung cancer are not random, but are associated with specific chromosomal instabilities that may be indicative of future carcinomas. Researcher Marileila Varella-Garcia, M.D., also of UCHSC, targeted these non-

random chromosomal changes in the study.

The investigators used a technique called spectral karyotyping (SKY) to examine the bronchial epithelium (BE) of 71 subjects—14 patients with lung cancer, 43 smokers at high risk for developing lung cancer and 14 healthy non-smokers—in the hope of identifying underlying genetic changes that might be hallmarks for cancer.

“It is critically important that we thoroughly understand the nature and timing of the cellular and genetic effects of tobacco smoke on BE in order to identify biomarkers and devise intervention strategies that might reduce the persisting morbidity and mortality from lung cancer,” said Dr. Varella-Garcia.

The researchers found a marked difference between the chromosomal abnormality index (CAI) of never-smokers and that of high-risk smokers and patients with lung cancer.

“There’s a tremendous amount of chromosomal damage in smokers who don’t yet have cancer,” said Dr. Franklin. “Chromosomal abnormalities were observed in 82 percent of high-risk smokers and in all patients with carcinoma, regardless of their self-reported tobacco exposure.” Patients with cancer and high-risk smokers had nearly 23 and 15 times more chromosomal abnormalities, respectively, than never-smokers.

The most common changes among patients with cancer and high-risk smokers were gains on chromosomes 5, 7, 8 and 18.

The results from SKY were confirmed by fluorescence in situ hybridization (FISH). The FISH technique offers a less comprehensive view of genetic changes, but unlike SKY, can detect genetic changes in interphase cells, which are readily available in sputum samples.

“Whereas SKY is not a practical tool to directly apply to sputum, it does identify candidate chromosomal sequences that could improve the sensitivity of a FISH probe set for sputum screening and risk assessment,” wrote Dr. Franklin. “Improvement in sensitivity and perhaps automated processing and analysis could move a FISH-based assay toward clinical application.”

The researchers noted that their pilot study could not affirmatively determine whether the changes were predictive of eventual cancer, but their data point to an important avenue for future research. “It will be necessary to study larger cohorts for a longer interval,” they wrote, concluding, “SKY FISH is a feasible technique for comprehensive evaluation of the chromosomal changes in nonmalignant bronchial epithelial cells of high-risk individuals.”

Source: American Thoracic Society