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## Lung alert

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### Airway epithelial gene expression to detect lung cancer in smokers

The sensitivity of bronchoscopy for detecting lung cancer ranges from 30% for small peripheral lesions to 80% for centrally located endobronchial lesions, necessitating further invasive diagnostic tests to try to establish the diagnosis. To address this diagnostic problem, the authors searched for profiles of gene expression in large airway epithelial cells knowing that cigarette smoke creates a field of injury in all airway epithelial cells exposed to it. In this study of 129 smokers with suspected lung cancer, the authors have identified an 80-gene biomarker that distinguishes smokers with and without lung cancer. They extracted RNA from normal large airway epithelial cells of 77 smokers and identified the 40 most frequently upregulated and 40 most frequently downregulated genes. This biomarker was then tested on samples from the remaining 52 smokers and on 35 samples from five different institutions.

The diagnostic sensitivity of bronchoscopy was increased to 94% by combining the traditional cytopathological testing of specimens with the gene biomarker, with a negative predictive value of 93% and a positive predictive value of 81%. In 92 out of 129 samples with non-diagnostic bronchoscopy, the gene biomarker had a diagnostic accuracy of 85%, sensitivity 89% and specificity of 83%. For early stage 1 lung cancer, the gene biomarker had a diagnostic sensitivity of about 90% compared with about 35% for routine cytopathological testing. Limitations of the study are that the gene biomarker cannot be used on its own owing to its low positive predictive value of 70%, and it does not contribute to the diagnostic aid of non-smokers who develop cancer.

This study shows that gene expression in normal large airway epithelial cells can be used as a lung cancer biomarker and improve the diagnostic sensitivity of bronchoscopy by supplementing the current cytopathological methods. Where facilities become available for performing such gene biomarker testing, further invasive testing may be avoided. A longitudinal study is warranted to find out if false positives on biomarker testing may represent smokers at higher risk of developing lung cancer.

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