

Genetic mutation associated with increased risk of lung cancer

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Carriers of a common genetic disorder previously linked to lung disease may have a 70-percent to 100-percent increased risk of lung cancer, according to a report in the May 26 issue of *Archives of Internal Medicine*.

The disorder, alpha1-antitrypsin deficiency (alpha1ATD), is one of the most common genetic conditions affecting the U.S. population and especially those of European descent, according to background information in the article. Individuals with two copies of the associated genetic mutation often develop emphysema at an early age. However, alpha1ATD carriers—those with only one copy of the mutated gene—do not normally have severe diseases related to alpha1ATD and may not be aware of their status. However, they may be more vulnerable to cancer-causing tobacco smoke than non-carriers.

Ping Yang, M.D., Ph.D., and colleagues at the Mayo Clinic, Rochester, Minn., tested for alpha1ATD carrier status in 1,443 patients with lung cancer. In addition, 797 community members without lung cancer and 902 siblings of lung cancer patients were tested as controls. Information was gathered about all participants' smoking history, demographic characteristics and family history of cancer.

A total of 13.4 percent of the lung cancer patients and 7.8 percent of unrelated controls were alpha1ATD carriers. When patients with lung cancer were compared to non-related controls, alpha1ATD carriers had a 70 percent higher risk of developing lung cancer than non-carriers. Comparing

patients with lung cancer to their cancer-free siblings, alpha1ATD carriers had twice the risk of developing lung cancer. The researchers estimated that alpha1ATD carrier status may account for 11 percent to 12 percent of the patients with lung cancer enrolled in the study.

Among those who had never smoked, alpha1ATD carrier status was associated with a 2.2-fold higher risk of lung cancer, with a 2-fold increased risk among light smokers and a 2.3-fold increased risk among moderate to heavy smokers. “Patients with a family history of lung cancer or other cancers in their first-degree relatives had a similar alpha1ATD carrier rate to those without such a family history, all significantly higher than the controls,” the authors write. “This finding suggests that increased lung cancer risk among alpha1ATD carriers is independent of a family history of cancer.”

“In summary, our findings demonstrate a paradigm in lung cancer etiology research and risk assessment that incorporates clinical and genetic markers for lung damage into a gene-environment interaction,” they conclude. “This knowledge may prove to be useful in further understanding the pathologic mechanisms of lung cancer development and in refining lung cancer risk assessment.”

Source: JAMA and Archives Journals

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