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Lung alert

Alpha-1-antitrypsin deficiency and increased lung cancer risk

Lung cancer development is a multifaceted process involving environmental and genetic factors, but their intricate interaction and extent of predisposition remains ill-defined. This study investigated the role of alpha$_1$-antitrypsin deficiency (α_1ATD), chronic obstructive pulmonary disease (COPD) and tobacco smoke exposure in lung cancer development in 1856 patients with lung cancer. The two control groups were free of any cancer and comprised 1585 community residents and 902 full siblings of patients. The α_1AT alleles were tested in 1443 patients, 797 unrelated controls and 902 full siblings. The carrier rate was 13.4%, 7.8% and 9.9%, respectively.

The findings suggest that α_1ATD carriers are at a 70–100% increased risk of lung cancer, particularly adenocarcinoma and squamous cell subtypes (adjusted for the effects of tobacco smoke exposure and COPD). Depending on smoking intensity, smokers were noted to have a 2–9-fold higher risk of lung cancer than never smokers. The study also confirmed that COPD, which conferred a greater than 6-fold risk of developing lung cancer, is an independent risk factor with an expected population attributable risk of 10–12%.

The study demonstrates complex gene-environment interplay in lung cancer development and indicates the potential benefit in identifying α_1ATD carriers who may be susceptible to carcinogens. The possible underdiagnosis of COPD, use of community-based controls and likelihood of ethnic stratification are potential limitations of the study. The authors suggest further studies to examine whether the excess risk of lung cancer in patients with COPD stems from emphysema, chronic bronchitis or both.

► Yang P, Sun Z, Krowka MJ, *et al*. Alpha1-antitrypsin deficiency carriers, tobacco smoke, chronic obstructive pulmonary disease, and lung cancer risk. *Arch Intern Med* 2008;**168**:1097–103

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