

SNPs of ABC transporter genes Linked to Lung Cancer Risk

Atlanta 2008/12/22 -Individuals with particular variants of certain genes involved in metabolizing the most potent carcinogen found in cigarette smoke have an increased risk of developing lung cancer. That is the conclusion of a new study published in the February 1, 2009 issue of *CANCER*, a peer-reviewed journal of the American Cancer Society. The study's results may help shed light on how lung cancer develops and could have important implications for preventing smoking-related cancers.

Tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) is a component of cigarette smoke that has been shown to cause lung cancer in rodents. Certain enzymes act to protect the body from this type of chemical by turning it into nontoxic forms or by transporting it from cells. For example, ATP-binding cassette transporters encoded by genes known as ABCB1 and ABCC1 are involved in eliminating carcinogens from the lungs, protecting them against inhaled toxins.

Researchers suspect that individuals with alterations in these genes might have an increased susceptibility to develop lung cancer. Recently, a team of scientists led by Dr. Daru Lu and Dr. Haijian Wang of the Fudan University in Shanghai identified common variants at the beginning and end of the ABC1 and ABCC1 genes. They then analyzed these variants in 500 patients with lung cancer and 517 cancer-free controls in a Chinese population.

The investigators found that certain variants were found much more often in individuals with lung cancer than in cancer-free controls. Patients who had the variant allele of either ABCB1 rs3842 or ABCC1 rs212090 had a significantly increased risk of developing lung cancer. The former variant was particularly associated with an increased risk of cancer in women and in individuals under age 60 years. It also was linked to a major type of lung cancer called adenocarcinoma.

Dr. Wang and his colleagues previously identified other common genetic variants associated with lung cancer risk in NNK disposition pathways, such as CYP2A13, the most active P450 for the phase metabolic activation of NNK (*Cancer Res* 2003; 63: 8057) and the receptor (ADRB2) in its non-genotoxic pathway (*Cancer Lett* 2006; 240: 297). This study shed new insight into the toxicogenomics of NNK and further supported the hypothesis proclaiming genetic components in the metabolism and disposition machines of NNK as modifiers of risk of lung cancer.

"Because tobacco smoking is the leading preventable cause of cancer and the cancer-prone genotypes of these genetic components are relatively prevalent in the human population, our findings have important implications for the prevention of tobacco smoking-related cancers," the authors write.

Article: "Genetic susceptibility of lung cancer associated with common variants in the 3' untranslated regions of the adenosine triphosphate-binding cassette B1 (ABCB1) and ABCC1 candidate transporter genes for carcinogen export." Haijian Wang, Guangfu Jin, Haifeng Wang, Gaifen Liu, Ji Qian, Li Jin, Qingyi Wei, Hongbing Shen, Wei Huang, and Daru Lu. *CANCER*; Published Online: December 22, 2008 (DOI: 10.1002/cncr.24042); Print Issue Date: February 1, 2009.

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