MedicalXpress

New research uncovers genetic link between emphysema, lung cancer

June 9 2011

A gene linked to emphysema also can be a factor for developing lung cancer unrelated to cigarette smoking, UT Southwestern Medical Center research indicates. Smoking was the only known risk factor previously associated with both diseases.

In the study, mice bred to have the human gene pleiomorphic adenoma gene-like 2 (PLAGL2) all developed emphysema, and by gender also developed lung cancer at rates as high as one in every six rodents. Although the new study showed PLAGL2 as a contributing factor in emphysema and lung cancer development, the diseases form in opposite ways. Emphysema arises from cell death or injury, while lung cancer involves uncontrolled cell growth.

"We think this gene induces emphysema by causing stem cells in the lung to die," said Dr. Jonathan Weissler, vice chairman of the department of medicine and chief of medicine at UT Southwestern University Hospital and senior author of the study, available online and due to be published in the journal *Lung Cancer* in October. "The cells that don't die through apoptosis would be more likely to have uncontrolled growth" and become cancerous, suggesting a genetic link between the diseases.

The gene is a known driver of several types of cancer. The degree to which PLAGL2 turns on, or is expressed, plays a role in cancer development. Previous research has demonstrated that female lung cancer patients with higher levels of gene expression had much poorer

survival rates.

Increased PLAGL2 expression also aggravates emphysema. In 2009, Dr. Weissler and UT Southwestern colleagues found that high expression of this gene led to enlarged airways (alveoli) in mice. Female mice in particular were more prone to develop emphysema.

"The mice in that study developed the same type of emphysema seen in smokers despite the fact they were not exposed to cigarette smoke," said Dr. Weissler, director of the James M. Collins Center for Biomedical Research.

The new study revealed higher incidence of lung cancer in male mice. Of two PLAGL2 mice groups tested, lung cancer developed in 12.5 percent and 18.5 percent of male mice. The rate for female mice was zero and 3.7 percent.

In human cases, the association between these two diseases also is stronger in men. One study showed that about 10 percent of patients with severe emphysema – all men – also had lung cancer. The reasons for these gender differences are as yet unknown, although this information eventually could be used to help identify patients at risk for cancer.

"PLAGL2 expression could be used as a marker for cells that are at risk of undergoing malignant transformation," Dr. Weissler said.

Other researchers involved in the study were lead authors Dr. Yih-Sheng Yang and Dr. Meng-Chun Yang, both former assistant professors of internal medicine at UT Southwestern.

Provided by UT Southwestern Medical Center