Cigarette smoking increases production of mucus in patients with bronchitis

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Cigarette smoking has been linked with overproduction of mucus associated with chronic bronchitis, according to a study conducted by researchers in New Mexico. The study indicates cigarette smoke suppresses a protein that causes the natural death of mucus-producing cells in the airways of bronchitis patients.

The findings were published online ahead of the print edition of the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

"Although it is known that chronic mucus secretion is a hallmark of chronic bronchitis, the mechanisms underlying this condition are largely unknown," said Yohannes Tesfaigzi, PhD, director of the COPD Program at Lovelace Respiratory Research Institute in Albuquerque. "This study shows that the airway cells that secrete mucus are sustained by cigarette smoke, which suppresses a cell death-inducing protein called Bik."

Chronic bronchitis is commonly associated with chronic obstructive pulmonary disease (COPD). Cigarette smoking is the leading cause of disease for 15□□ million individuals with COPD in the United States alone and for over 200 million people worldwide.

"Previous studies have shown overproduction of mucus cells is common in the large and small airways of cigarette smokers," Dr. Tesfaigzi said. "This overproduction in the small airways is responsible for airway

obstruction and reduced lung function and in the pathogenesis of acute exacerbations of COPD.

"Our previous studies show that following inflammatory responses, up to 30 percent of cells lining the airways undergo death and return to the original cell numbers," he continued. "This cell death is aided in part by proteins, including Bik. Disruption of this recovery process may lead to persistent elevation of mucus cell numbers and contribute to airway obstruction found in chronic lung diseases such as chronic bronchitis.

"Based on these earlier findings we wanted to determine if Bik may be responsible for sustained mucus cell growth in the airways of cigarette smokers," he said.

To test their hypothesis, the researchers examined both human airway tissue samples and mouse models. Human samples were derived from autopsy tissues and from bronchial brushings taken from individuals with chronic bronchitis as well as healthy controls. Chronic bronchitis was defined as a daily cough with phlegm production for 3 consecutive months, 2 years in a row.

Mice were exposed to cigarette smoke for six hours per day, five days per week for three weeks. Following exposure, lung tissue samples were collected and examined for the presence of Bik.

The researchers determined Bik was significantly reduced in bronchial brushings of patients with chronic bronchitis compared to non-diseased controls. Examination of autopsy tissues confirmed the finding. Mice exposed to cigarette smoking also had significantly reduced Bik levels and increased numbers of mucus-producing cells.

In another arm of the study, mice exposed to cigarette smoke were subsequently exposed to filtered air for 60 days and evaluated for Bik

levels to determine whether Bik remains suppressed even after cessation of cigarette smoking. They found mice exposed to cigarette smoke still exhibited significantly lower levels of Bik, even after being exposed to filtered air.

"We found that cigarette smoke suppresses Bik levels in humans and in mice models, and mucus cells increased threefold in mice exposed to cigarette smoke," he said. "Moreover, the mouse study suggests that Bik remains suppressed in former cigarette smokers that have persistent chronic bronchitis. In humans, Bik was reduced even more in former smokers who had chronic bronchitis compared to former smokers without.

"The possible therapeutic value of these findings was tested by restoring Bik levels in the airways of cigarette smoke-exposed mice or human airway epithelial cells using genetic approaches," Dr. Tesfaigzi said. "This approach reduced the epithelial cells in cigarette smoke-exposed mice.

"These studies lay the foundation to investigate therapies that may restore expression of Bik and reduce the numbers of mucus-producing cells," he added. "This method may reduce excess secretion of mucus and the airway blockages in patients with chronic bronchitis."

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