Researchers identify novel approach to study COPD and treatment efficacy

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(Medical Xpress)—Researchers from Boston University School of Medicine (BUSM) have pinpointed a genetic signature for chronic obstructive pulmonary disease (COPD) from airway cells harvested utilizing a minimally invasive procedure. The findings provide a novel way to study COPD and could lead to new treatments and ways to monitor patient's response to those treatments. The study is published online in the *American Journal of Respiratory and Critical Care Medicine*.

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease that leads to the loss of lung function primarily caused by cigarette smoking. It causes coughing, wheezing, shortness of breath, chest tightness and other symptoms that make it difficult to breathe. While there are treatments and lifestyle changes that can help people cope with COPD, there currently is no cure and there are no effective therapies to reduce the rate of lung function decline. According to the National Institutes of Health's National Heart, Lung, and Blood Institute (NHLBI), which partially funded the study, COPD is the third leading cause of death in the United States, resulting in approximately 135,000 deaths each year.

"There have been limited molecular studies of COPD given the inaccessibility and invasiveness of obtaining lung tissue," said Katrina Steiling, MD, MSc, assistant professor of medicine at BUSM who served as the study's first author. The researchers hypothesized that while COPD primarily affects the tissue deep within the lung, the effects of

COPD might be detectable in relatively accessible tissue throughout the respiratory tract. This echoes previous work they had done that found that cancer found deep in the lung could be detected by cancer-specific patterns of gene expression in the largest airways connected to the windpipe, far from the tumor.

To examine their hypothesis, the research team used airway cells obtained during a bronchoscopy, a procedure that involves putting a small camera into the airway through the nose or mouth. During the procedure, which can be done while a patient is awake under local anesthesia or moderate sedation, a cytology brush is used to gently scrape the sides of airways to collect cells.

They examined 238 samples from current and former smokers that had been collected by Stephen Lam, MD, a collaborator from the University of British Columbia. Eighty seven of the samples were from patients who had been diagnosed with mild to moderate COPD based on their lung function. The other 151 samples represented patients who did not have COPD based on these criteria.

When the researchers compared the airway samples from both groups, they found that 98 genes were expressed at different levels in those diagnosed with COPD compared to those without COPD. In order to determine how similar the airway cell changes were to lung tissue cells, the researchers compared their results with previously published findings on the gene expression changes associated with COPD in lung tissue. The results of the comparison demonstrate that the changes that occur in the airway cell samples in those diagnosed with COPD were similar to the changes in lung tissue cells of individuals with the disease despite the airway cells coming from regions of the lung not thought to be altered by disease.

"Our data shows that there are consistent gene-expression changes that

occur in both airway and lung tissue cells in individuals with COPD," said Avrum Spira, MD, MSc, Alexander Graham Bell professor of medicine and chief of the division of computational biomedicine at BUSM who served as one of the senior co-authors of the study. Spira also is a physician in the pulmonary, critical care and allergy department at Boston Medical Center.

To investigate the effects of treatment on the COPD-associated gene expression changes, the researchers collaborated with a team led by Maarten van den Berge, MD, PhD, from the University of Groningen Medical Center in the Netherlands that had collected airway cells from COPD patients before and after they started steroid therapy. They found that the expression of some genes that changed due to COPD reversed their expression after treatment and started to look more like the levels seen in current or former smokers without COPD.

"Part of the COPD 'signature' reverses with therapy, suggesting that examining airway cells might be a minimally invasive tool for monitoring the disease and evaluating the response to therapy more quickly in order to determine the best course of treatment for each individual patient," said Marc Lenburg, PhD, associate professor in computational biomedicine and bioinformatics at BUSM and the study's other senior co-author.

"Studying COPD using the large airway opens up some really exciting new avenues of research that could also improve care for patients with COPD," said Spira. "While we are still at an early stage, I envision being able to examine airway cells from my patients with COPD to determine what is causing the disease and, from that information, recommend a more specific and effective treatment."

Provided by Boston University Medical Center

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