Cell division abnormality contributes to inflammation in COPD

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Changes in the ability of lung cells to divide may play a role in initiating or prolonging lung tissue inflammation, a hallmark of chronic obstructive pulmonary disease (COPD), according to a study conducted by researchers in France.

The results will be presented at the ATS 2011 International Conference in Denver.

"We found that lung tissue cells of patients with COPD had an impaired ability to divide, or had lost their ability to divide," said lead author Valerie Amsellem, MD, PhD, professor of medicine at the National Institute of Health and Medical Research (INSERM) in Creteil, France. "This phenomenon, called senescence, affects several types of cells that build the lung. In addition, we found that these cells change their behavior by producing different molecules that could contribute to inflammation."

COPD is associated with smoking and occurs much more commonly in individuals as they grow older. Dr. Amsellem wanted to determine if the aging process of cells contributes to the sustained lung inflammation associated with COPD.

During its normal life cycle, a cell will divide many times; however, its ability to divide decreases as it ages. This cellular aging process, or senescence, can vary by cell, and can also be affected by disease processes. In this study, the researchers looked specifically at endothelial cells, which border the tiny blood vessels in the lungs and create a barrier between blood and tissue.

Endothelial cells were collected from 15 patients with COPD and 15 age- and sex-matched control subjects, who were smokers but did not have COPD. Laboratory analysis of the cells revealed a higher percentage of senescent endothelial cells in patients with COPD when compared to controls. In addition, endothelial cells from COPD patients displayed accelerated senescence, meaning they lost their ability to divide compared to endothelial cells from control subjects. Senescent cells from COPD patients also produced greater numbers of molecules, which are associated with increased and persistent inflammation, than their control counterparts.

"We found that endothelial cells from the lungs of COPD patients displayed more characteristics of senescence than cells from patients not affected with COPD, and we also showed that it is the senescence of these cells that creates an inflammatory context that could contribute to lung inflammation which is seen in COPD," Dr. Amsellem said.

Although an increase in senescent characteristics was expected, Dr. Amsellem said the finding that the senescent process appeared to contribute to unresolved inflammation was not.

"We expected to find senescence characteristics in the cells of COPD patients," Dr. Amsellem said. "However, the fact that senescent endothelial cells released factors promoting sustained inflammation was a novel finding.

"The fact that it is the accelerated aging phenomenon of cells that contributes to inflammation will open a new therapeutic strategy to cure chronic inflammation in COPD disease," she added.

Future research will focus on strategies to limit senescence of cells associated with inflammation, and to understand how senescence of endothelial cells affects other cells involved in conditions, which may occur in patients with COPD, such as cardiovascular disease.

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