

New technique reduces tobacco smoke damage to lungs in mice

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Researchers in Australia have demonstrated that blocking a certain protein can reduce or prevent cigarette smoke-induced lung inflammation in mice. Inflammation underlies the disease process of chronic obstructive pulmonary disease (COPD) and many other smoking-related ailments.

The findings have been published online ahead of print publication in the American Thoracic Society's *American Journal of Respiratory and [Critical Care Medicine](#)*.

Cigarette smoking causes [lung inflammation](#), which can lead to oxidative stress, emphysema, small airway fibrosis, mucus hypersecretion and progressive airflow limitation. Since the inflammatory reaction to cigarette smoke responds poorly to current anti-inflammatory treatments, there is intense research to identify more effective therapies for cigarette smoke-induced lung damage.

Granulocyte macrophage-colony stimulating factor (GM-CSF) is of special interest because it governs the growth, activation and survival of leukocytes directly implicated in the pathogenesis of COPD.

Cigarette smoke triggers the release of GM-CSF and other cytokines and chemokines which cause activation and recruitment of more inflammatory cells into the lung, thereby perpetuating the inflammatory response and exacerbating ongoing inflammation. These activated and recruited inflammatory cells also release proteases such as matrix

metalloproteinase (MMP)-12, which destroy the lung tissue, resulting in emphysema.

The research team from the University of Melbourne set out to determine whether blocking GM-CSF could reduce the inflammation and other deleterious effects of [cigarette smoke](#) exposure in mice.

To do so, they exposed a group of mice, half of which had been treated with a GM-CSF blocking agent, anti-GM-CSF, and half of which were controls, to the equivalent of nine cigarettes of smoke each day for four days. At the end of four days, the mice were killed and their lung tissue was examined for the presence of inflammatory cells.

"We found that anti-GM-CSF strongly reduced the number of potentially harmful white blood cells that infiltrate the lung after smoke exposure, as well as inhibiting the pro-inflammatory cytokine tumor necrosis factor (TNF)- α , the chemokine macrophage inflammatory protein-2 (MIP-2), which coordinates the movement of white blood cells into the lung. It also inhibited the protease MMP-12, which is known as one of the main enzymes able to destroy [lung tissue](#)," said lead researcher on the study, Ross Vlahos, Ph.D., a senior research fellow with the lung disease research group at the University of Melbourne. "Cigarette smoke-exposed mice that were treated with an anti-GM-CSF had significantly less lung inflammation in comparison to untreated mice. This indicates that GM-CSF is a key mediator in smoke-induced lung inflammation and its neutralization may have therapeutic implications in diseases such as COPD."

These results, though preliminary, may illuminate a new pathway toward fighting smoke-related disease, specifically COPD. "Short-term models often translate into benefits in longer-term models. We still need to develop new methods and agents to test this idea long term and we also need to learn if it is effective in reversing longstanding disease,"

explained Dr. Vlahos.

In future research, Dr. Vlahos hopes to test whether GM-CSF could be a key target in other disease processes. "We want to understand exactly how blocking GM-CSF alters disease processes at the cellular and molecular levels so we can use this fine detail to make other treatments."

But this research is no free pass for patients to continue smoking, he warned: "Our treatment deals with cigarette smoke-induced lung inflammation involved in COPD, not cancer and other smoking-related ailments. Quitting remains the best and only cure for smoking-related lung disease."

Provided by American Thoracic Society

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