

Findings on pollution damage to human airways could yield new therapies

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Researchers from Duke University Medical Center have identified how nanoparticles from diesel exhaust damage lung airway cells, a finding that could lead to new therapies for people susceptible to airway disease.

The scientists also discovered that the severity of the injury depends on the genetic make-up of the affected individual.

"We gained insight into why some people can remain relatively healthy in polluted areas and why others don't," said lead author Wolfgang Liedtke, M.D., Ph.D., assistant professor in the Duke Department of Medicine and an attending physician in the Duke Clinics for Pain and Palliative Care.

The work was published on-line in the journal <u>Environmental Health</u> <u>Perspectives</u> on Jan. 18.

<u>Diesel exhaust</u> particles, a major part of urban smog, consist of a carbon core coated with organic chemicals and metals. The Duke team showed that the particle core delivers these <u>organic chemicals</u> onto brush-like surfaces called cilia, which clear mucus from the airway lining.

Contact with these chemicals then triggers a "signaling cascade," as the cells respond.

In some patients, who have a single "letter" difference in their DNA, a circuit called the TRPV4 ion channel signals more strongly in response



to the pollutants. Previous research showed that this <u>gene variant</u> makes humans more liable to develop chronic-obstructive disease (COPD), and the current study provides an explanation for this observation.

About 75 percent of people have the version of the gene MMP-1 that leads to greater production of the molecule MMP-1 mediator, which destroys lung tissue. This genetic make-up allows for a turbo-charged production of MMP-1, which damages airways and lungs at multiple levels, Liedtke said.

A more fortunate 25 percent of people escape this high level of production of MMP-1, which may be reflected in the fact that certain individuals can better manage the effects of air pollution without grave airway damage.

The injurious molecule MMP-1 is known to enhance the development of certain devastating lung diseases, such as chronic-obstructive pulmonary disease (COPD), a top-ten ailment in world-wide morbidity and mortality, according to the World Health Organization. The devastating, tissue-destructive actions of MMP-1 can also lead to lung emphysema, which is chronic reduction of the lung surface dedicated to gaseous exchange, and to the spread of lung cancer cells, through migration of these cells from <u>lung tissue</u> that has become cancerous.

The new study also provides a direction for developing therapeutics for those who are genetically more susceptible to air pollution and airway damage, Liedtke said. "If we can find a way to stop the hyperactivation of MMP-1 in response to diesel-engine exhaust particles and reduce it to levels that the airways can manage, then we will be helping a large number of people worldwide," he said. "It is attractive to envision inhaled TRPV4 inhibitor drugs, rather than swallowing a pill or taking an injection. I envision this as rather similar to inhaled drugs for allergic airway disease that are currently available."



Provided by Duke University Medical Center

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