

# Mapping the destructive path from cigarette to emphysema

January 18 2012

---

From the cherry red tip of a lighted cigarette through the respiratory tract to vital lung cells, the havoc created by tobacco smoke seems almost criminal, activating genes and portions of the immune system to create inflammation that results in life-shortening emphysema, said researchers led by those at Baylor College of Medicine and the Michael E. DeBakey Veterans Affairs Medical Center.

In a report online in the journal [\*Science Translational Medicine\*](#), the scientists, including two from The University of Texas MD Anderson Cancer Center, described the track the toxic smoke takes through the tissues and how they accomplish their destructive work.

"It's like walking into a crime scene," said Dr. Farrah Kheradmand, professor of medicine and immunology at BCM and a senior author of the report. In their current work, the scientists took [cells](#) present in the "crime scene" apart, piece by piece to elucidate what occurred when, and how.

It is a complicated story that took more than four years for her, her co-senior author Dr. David Corry and members of their laboratories and colleagues in the Dan L. Duncan Cancer Center at BCM to unravel, she said. Corry is professor and chief of the section of immunology, allergy and rheumatology in the department of medicine at BCM and a member of the faculty at the Michael E. DeBakey VA Medical Center.

"Previously, emphysema was thought to be a non-specific injurious

response to long-term [smoke exposure](#)," she said. "These studies show for the first time that emphysema is caused by a [specific immune response](#) induced by smoke."

"It is a combination of little genes affected by an epigenetic factor," she said. Epigenetics are factors that affect the way genes are expressed after DNA forms. [Cigarette smoke](#) is an environmental epigenetic factor.

"DNA is written in pen," said Kheradmand, using a metaphor.

"Epigenetics is written in pencil. If you have enough genes affected by epigenetic factors strung together, it can tip you over into [lung damage](#) and emphysema. The inflammation that drives emphysema could also drive cancer development, a testable hypothesis that we have begun to pursue."

This study showed that the cigarette recruited antigen-presenting cells (cells that orchestrate the immune system's response to antigens) as co-conspirators in the lung-destroying crime, using specific genes that regulate proteins in their deadly role.

To uncover the cause of tobacco- induced emphysema, they studied mice exposed to conditions that closely simulated how humans smoke. These animals developed the lung disease in three to four months. Certain inflammatory cells and genes proving crucial to the process, she said.

For example, the cytokine interleukin-17 was critical. "When we removed IL-17 from the mice, they did not develop emphysema in the same time span," she said. "The number of a type of immune cell – the gamma delta T-cell – would increase dramatically in the crime scene of the lung, she said."

"But when we took them out, the inflammation worsened. The gamma

delta T-cells went there to dampen the inflammation," she said. "When they become overwhelmed, the disease ensues."

They confirmed that a subset of antigen-presenting cells (cells that present antigen to activate the immune system) are the key to orchestrating the disease. They had first found these cells in studies of human lung tissue. Then, they duplicated that finding in mice.

Dr. Ming Shan, now a postdoctoral associate in Kheradmand's laboratory, then took the cells out of the lungs of the mice with disease and transferred into mice who had never been exposed to cigarette smoke. After three months, these mice showed inflammatory signs indicating that they were on the way to developing lung damage and emphysema.

When they analyzed "gene chips" to screen the disease-causing antigen-presenting cells recovered from lungs with emphysema, they uncovered the gene for osteopontin, which promotes initiation of the inflammatory cascade that damages lungs. Mice that lacked this gene were resistant to [emphysema](#), said Kheradmand.

Provided by Baylor College of Medicine

Citation: Mapping the destructive path from cigarette to emphysema (2012, January 18) retrieved 20 March 2024 from

<https://medicalxpress.com/news/2012-01-destructive-path-cigarette-emphysema.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--