Dendritic cells spark smoldering inflammation in smokers' lungs

October 28 2009

Inflammation still ravages the lungs of some smokers years after they quit the habit. What sparks that smoldering destruction remained a mystery until a consortium of researchers led by Baylor College of Medicine found that certain dendritic cells in the lung - the cells that "present" a foreign antigen or protein to the immune system - provoke production of destructive T-cells that attack a key protein called elastin, leading to death of lung tissue and emphysema.

A report of their work appears in the current issue of *Science Transformational Medicine*. The National Heart, Lung and Blood Institute estimates that 2 million Americans have emphysema, most of them over the age of 50 years. People with emphysema find it harder and harder to breathe as the lung's air sacs or alveoli are destroyed, causing holes in the lung and blocking airways. They have difficulty exchanging oxygen as their lungs become less elastic. Cigarette smoking is the greatest risk factor for the disease that contributes to as many as 100,000 deaths each year.

In previous work, Dr. Farrah Kheradmand, associate professor of medicine - pulmonary and immunology at BCM, and colleagues had shown that T-helper cells and some enzymes in the lung destroyed tissue in the lungs of emphysema patients. She credits BCM graduate student Ming Shan with pushing the project forward with the work in the current report.

She and her colleagues found that a subset of antigen-presenting cells in

the lung are programmed to turn peripheral blood cells into the cells that are activated and are associated with autoimmune inflammation. They also found that elastin peptides can activate T cells -a sign that elastin is acting as an auto-antigen.

"This has implications for something that is important and biologically relevant," said Kheradmand. "Smokers are also at risk for diseases of the blood vessels such as the carotid artery and aorta. These blood vessels are also enriched in elastin. We believe that particular cells circulating in the body could react to elastin molecule at these remote sites."

This may help explain some of the cardiovascular and other complications associated with smoking tobacco. For example, skin is rich in elastin. The skin of smokers loses elasticity.

"We believe that this systemic inflammation that may initially affect the lung could also affect other parts of the body," she said.

She and fellow senior author Dr. David Corry, professor of medicine - pulmonary and immunology, and her colleagues used lung tissue taken from emphysema patients who were undergoing surgery anyway to determine which cells are present and their functions in the lung.

"These live cells are the center of what we studied," she said.

She and her colleagues found that some patients did not have the elastin-specific cells in their lungs, even though they had smoked.

"The Holy Grail is to find smokers who are destined to develop auto-reactive cells before the disease is fully manifested," she said. She said they hope to come with a test for T-cells that attack elastin that could be used in the doctor's office. However, she said, such a test would only identify patients at higher risk for emphysema and other elastin-

associated diseases. It would not identify people at higher risk of lung cancer, for example.

"It is not a good excuse to smoke or continue smoking," she said.

More information: stm.sciencemag.org/

Source: Baylor College of Medicine (news : web)