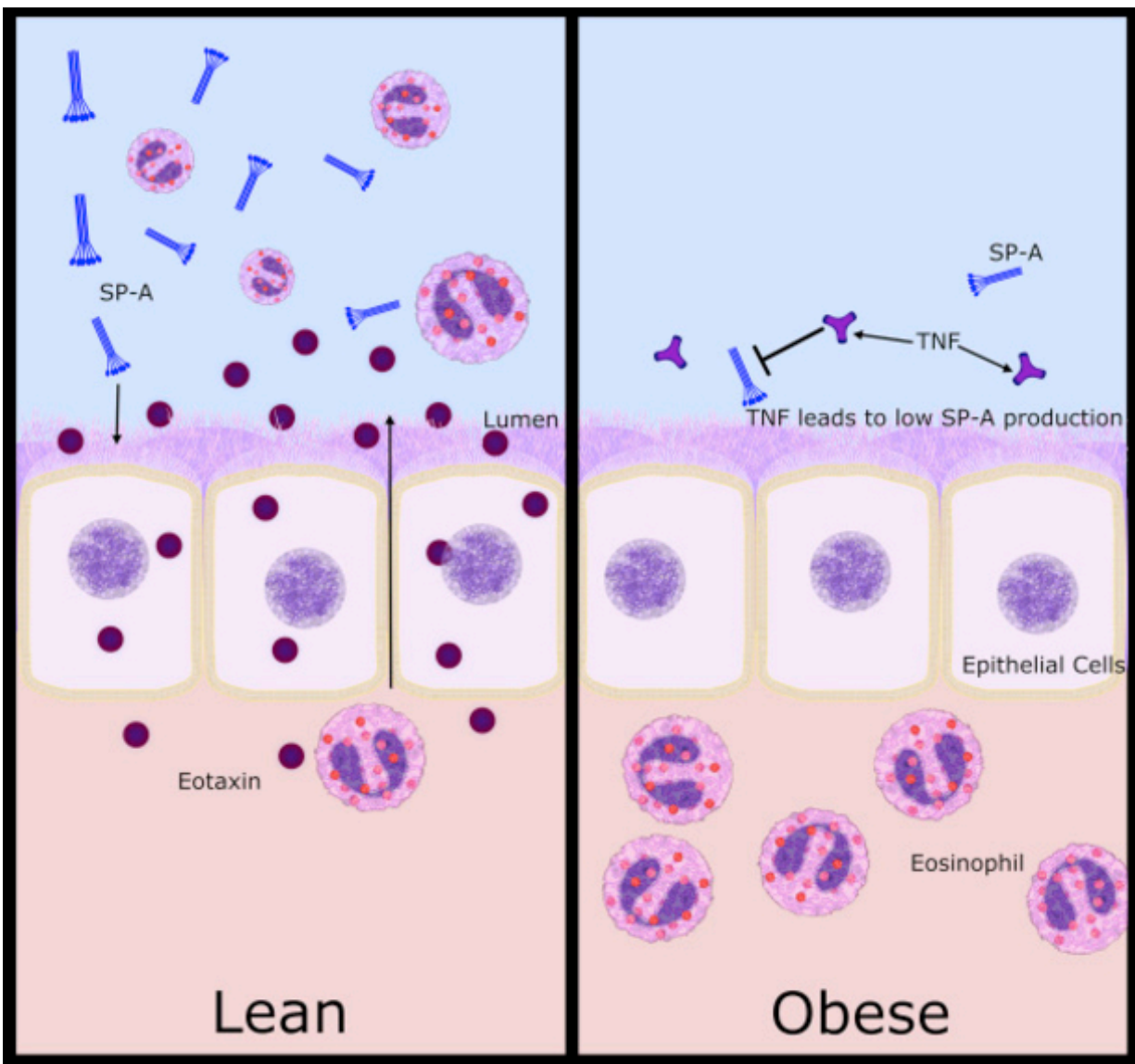


Study finds molecular explanation for struggles of obese asthmatics

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Obese asthmatics have increased TNF-alpha levels, which, in part, leads to

decreased SP-A secretion. Subsequently, these individuals have enhanced eosinophilia. Credit: University of Arizona

A large, bouquet-shaped molecule called surfactant protein A, or SP-A, may explain why obese asthma patients have harder-to-treat symptoms than their lean and overweight counterparts, according to a new study led by scientists at the University of Arizona and Duke University. The results were published in a recent edition of the *Journal of Allergy and Clinical Immunology*.

The study, titled "Obese Asthmatics Have Decreased Surfactant Protein-A Levels: Mechanisms and Implications," compared SP-A levels in lean and overweight asthmatics against SP-A levels in obese asthmatics (those with a [body mass index, or BMI, over 30](#)). Obese individuals had significantly less of the protein.

To understand why the lack of the protein is such a problem for those with asthma, one must first understand the function of SP-A, a powerhouse of a protein that helps curb the lungs' responses to environmental insults such as air pollution. It also regulates the numbers and locations of disease-fighting white blood cells called eosinophils. Without enough SP-A to rein them in, one ends up with too much of a good thing. The eosinophils collect in the lungs and wreak havoc.

The team included UA researchers Dave Francisco, Kenneth Addison, Akarsh Manne, William Pederson, Dr. Monica Kraft and Julie Ledford.

Kraft, department chair and professor of medicine, and Ledford, an assistant professor of medicine, are members of the UA's BIO5 Institute. They began this research in 2010, when Ledford was a postdoctoral fellow at Duke University and Kraft was chief of pulmonary and critical

care medicine.

At that time, SP-A levels in asthmatic patients were relatively well studied, yet little understood. The literature was shaky. Some research showed that asthmatic patients have more SP-A than healthy individuals, others found they have less, and still others found they had the same amount. Using about 50 samples from the patients of medical doctors, including Kraft and Ledford, also got mixed results.

"I saw a really wide discrepancy in levels," Ledford said. "My results matched everything that had been published, so Monica and I looked at patient demographics to see if anything stood out."

There in the data, Ledford saw it plain as day: People with especially low levels of SP-A had especially high BMIs. It was the first time anyone had made the connection.

This latest study, with data from 55 individuals, shows the same connection Ledford made years ago. The study also provides insights on what is driving that stark difference in SP-A levels between [obese individuals](#) and others.

It starts with something called cytokines, little proteins made by cells in the immune system, giving other cells a signal to take some kind of action. By moving out of a cell, one cytokine called tumor necrosis alpha, or TNF-a, tells other cells to activate the immune system. Obese individuals often have increased amounts of TNF-a.

If you have enough of it, Ledford explained, TNF-a can actually suppress SP-A. And according to this study, in obese asthmatics, it does just that.

"These results are eye-opening in that we're finding out potentially why

obese asthma patients don't respond as well to treatments as other asthmatic patients. It could be due to the lack of this important immunoregulatory protein," Ledford said. "I hope this study will lead to better patient care for this group of people.

"SP-A is well known to fight pathogens, so with pretty much any lung infection, someone with less SP-A would be at a higher risk for complications," she said, adding that across all demographics of asthmatic patients, SP-A doesn't work as well as it should to begin with.

Ledford and Kraft are working to translate this information into a new therapy.

"The active piece of surfactant protein A is, we think, 10 to 20 amino acids. We're putting that piece of it into an inhaler as a delivery," Ledford said.

They are working with [Tech Launch Arizona](#), the UA office that commercializes inventions stemming from research, to develop and license the treatment for those with asthma and other respiratory diseases.

"Fundamentally, we do research to address grand challenges facing our society," said Kimberly Andrews Espy, the UA's senior vice president for research. "And by taking this groundbreaking discovery from the lab to the marketplace, Drs. Ledford and Kraft will improve the lives of patients with difficult-to-treat asthma. I am so proud of their work and of the impact it will have for so many. The University of Arizona is an international leader in research in airway diseases, and Dr. Ledford's and Dr. Kraft's work adds to our record of accomplishment."

Ledford and Kraft are now working to further understand what factors, beyond TNF-a, might lead to decreased levels of SP-A. They also would

like to study SP-A levels in bariatric [patients](#) before and after their weight-loss surgeries.

Said Ledford: "I'm getting to see where and how my work in the lab can affect patient outcomes and, as a scientist, that's the best reward one can get."

More information: Njira Lugogo et al. Obese asthmatic patients have decreased surfactant protein A levels: Mechanisms and implications, *Journal of Allergy and Clinical Immunology* (2017). [DOI: 10.1016/j.jaci.2017.05.028](#)

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