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Dr. Monica Kraft

\$7 Million NIH Grant to UA College of Medicine - Tucson Aimed at Helping Asthma Sufferers Reduce Severe Attacks

Led by Monica Kraft, MD, at the University of Arizona College of Medicine - Tucson, researchers will use the National Institutes of Health grant to conduct a five-year study, "Dysfunction of Innate Immunity in Asthma," to investigate the interrelationship of genetic mediators to reduce lung inflammation and attacks in asthma patients.

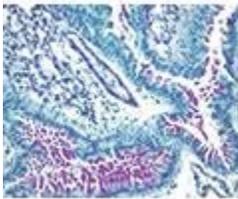
About 25 million people in the United States—7 million of them children—suffer from asthma. A five-year, \$7 million National Institutes of Health grant awarded recently to **Monica Kraft, MD**, an internationally renowned physician-scientist who specializes in translational asthma research at the [University of Arizona College of Medicine – Tucson](#) and the UA Health Sciences' [Asthma and Airways Diseases Research Center](#), will seek a better understanding of mediators that help control lung inflammation and improved therapies to reduce severe attacks in those with asthma.



Dr. Julie Ledford and Akarsh Manne, an associate scientific investigator for Dr. Kraft, discuss results from a recent genetic analysis of samples in her lab.

Funded through the National Institute of Allergy and Infectious Diseases (NIAID), the grant will support a research study, "Dysfunction of Innate Immunity in Asthma," with three projects, including analysis of human samples of people with asthma and investigation of genetic markers related to dysfunctional immune response mechanisms in asthma. The goal is to develop a better understanding of those mechanisms and refine novel therapies to moderate or eliminate asthma attacks and enable asthma sufferers to breathe easier.

Analysis will focus on dysfunctional single nucleotide polymorphisms (SNPs or "snips") of [surfactant protein A \(SP-A\)](#), a lipid constituent of surfactant known as POPG (palmitoyl-oleoyl-phosphatidylglycerol) and Toll-like receptor interacting protein (Tollip). Surfactant helps to open up aveolar sacs in the lungs and change surface tension so lungs can expand. SP-A, POPG and Tollip act as mediators, signaling synergistically which foreign irritants or conditions in the lungs to attack or not. Each perform critical negative regulatory functions interacting cooperatively to offer protection from allergic inflammation and viral exacerbations of asthma—but, when impaired, cause more acute reactions in asthma sufferers.



Transmission electron microscope image of a thin section of the

"We'll look at how certain airway cells handle infectious agents in the setting of allergic inflammation in asthma," Dr. Kraft said. "We've found, in humans, not all SP-A is created equal. The same holds true for Tollip. Depending on

alveolar sac region of the lung. The cell shown has vesicles that contain surfactant, a macroaggregate of phospholipids and proteins that help with breathing.

the genetics of your SP-A or Tollip, their function can be impaired. So, if you have these impaired or dysfunctional aspects of host defense and suffer from asthma, the combination can be very detrimental—leading to more allergic inflammation and asthma attacks.”

“UAHS has some of the best minds in the world working to treat and cure asthma, and this grant from NIH further strengthens the research under way at the UAHS Asthma and Airway Diseases Research Center,” said UA President **Ann Weaver Hart**. “We are incredibly proud of this work and the good outcomes it will help create for patients.”

“This research also dovetails well into the mission of the recently funded [NIH Precision Medicine Initiative® Cohort Program](#), which includes UAHS, to improve prevention and treatment of disease based on individual needs and diverse populations,” said **Joe G.N. “Skip” Garcia, MD**, UA senior vice president for health sciences, the Dr. Merlin K. DuVal Professor of Medicine and an elected member of the National Academy of Medicine.

Study participants will be recruited through the UAHS Asthma and Airway Diseases Research Center, with assistance from allergist **Tara Carr, MD**, and pulmonologist **Cristine Berry, MD, MHS**, both UA assistant professors of medicine.

For SP-A lab analysis, Dr. Kraft will work with **Julie Ledford, PhD**, a UA assistant professor of medicine and immunobiology, who also has worked with Dr. Kraft to develop a therapeutic treatment involving small functional peptides of SP-A to correct function of a genetic variant in asthmatics.

Two other projects—analysis of the lipid POPG and protein Tollip—will be coordinated by **Hong Wei Chu, MD**, and **Dennis R. Voelker, PhD**, of National Jewish Health, an academic medical research facility associated with the University of Colorado Denver.

Drs. Ledford, Chu and Voelker are longtime collaborators with Dr. Kraft when she was at Duke University and the University of Colorado before joining the UA in 2014 as chair of the UA Department of Medicine—the largest department at the College of Medicine – Tucson—and the Robert and Irene Flinn Endowed Chair of Medicine.

The study is part of NIAID’s U19 Cooperative Research Program, which involves about a dozen [Asthma and Allergic Diseases Cooperative Research Centers](#) across the country—of which the UA is the newest.

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Contact: [David Mogollón](#), 520-626-1137

