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LJI scientists uncover immune cells that may lower airway allergy and asthma risk

Study opens up new path to research to fighting allergic diseases

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LA JOLLA—The world is full of house dust mites. Do some cleaning, and you'll probably stir some up. While everyone has immune cells capable of reacting to common allergens like house dust mites, most of us have no allergic symptoms.

Still, many people do react with the typical allergic symptoms: sneezing, a runny nose, and itchy, swollen nasal passages. Others have a much more severe reaction: a life-threatening asthma attack.

To treat the root cause of allergies and asthma, researchers need to know exactly what sets these patients apart from healthy individuals.

In a new [Science Immunology study](#), published on June 12, 2020, scientists at La Jolla Institute for Immunology (LJI) offer a clue to why non-allergic people don't have a strong reaction to house dust mites. They've uncovered a previously unknown subset of T cells that may control allergic immune reactions and asthma from ever developing in response to house dust mites—and other possible allergens.

"We discovered new immune cell subsets and new therapeutic opportunities," says [Grégory Seumois, Ph.D.](#), instructor and director of LJI's Sequencing Core and co-leader of the new study. "This new population of cells could be one, out of many unknown mechanisms, that explains why healthy people don't develop inflammation when they breathe in allergens."

"The study highlights the power of unbiased single-cell genomics approaches to uncover novel biology," says LJI Professor [Pandurangan Vijayanand, M.D. Ph.D.](#), senior author of the new study.

The study builds on the Vijayanand lab's expertise in linking gene expression to disease development. The team also took advantage of the [Immune Epitope Database](#), an LJI-led

resource that houses information on how the immune system interacts with allergens like house dust mites.



House dust mites are everywhere. Image: La Jolla Institute for Immunology

Why house dust mites? These microscopic critters are hard to avoid, which means nearly everyone has been exposed. Even in people without a house dust mite (HDM) allergy, the immune system is likely to react in some way as it learns to recognize HDM molecules. This makes HDM a useful model for studying what causes allergies and asthma attacks.

The LJI team used a technique part of the “genomic revolution” arsenal of tools, called single-cell RNA-seq (or single cell transcriptomics) to see exactly which genes and molecules specific T cells produce in response to HDM allergens. They tested cells from four groups of people: people with asthma and HDM allergy, people with asthma but no HDM allergy, people with only HDM allergy, and healthy subjects.

Their analysis suggests that a subset of helper T cells, called interleukin (IL)-9 Th2 expressing HDM-reactive cells, is more prevalent in the blood of people with HDM-allergic asthma compared with those who are only allergic to HDM. Further analysis suggested that those IL9-TH2 cells are enriched in a group of molecules/genes that increased the cytotoxic potential of those cells. In other words, those specific T cells could kill other cells and drive inflammation.

In contrast, another subset of T cells stood out in the non-allergic subjects. These T cells express an “interferon response signature” and were enriched for a gene that encodes a protein called TRAIL. The work done by Seumois and his colleagues suggest that TRAIL could be important because it could dampen the activation of helper T cells.

This finding may mean that people with this specific cell population could have less T-cell driven inflammation in response to HDM allergens. At last, this could provide a clue to why some people develop allergies and asthma while others do not.

“Now if functional studies confirm this dampening effect, we’re curious if there is a way to boost the activation of these T cells or induce their proliferation in asthmatic or allergic populations,” says Seumois. “Can we act on those cells very early on, before asthma has developed?”

For example, genomics studies like this one may someday help identify children at risk of developing asthma and allergies. Early detection could open the door to preemptively acting on immune cells before development of allergy and asthma.

While Seumois emphasizes that there is much more work to be done, he says the transcriptomic method used for this study could accelerate future asthma and allergy research. “This is the first large-scale, single-cell, RNA-seq transcriptomic analysis for LJI,” says Seumois. “Now that we have developed the bench know-how and analysis pipeline, it could be applied to many diseases.”

The study, titled [“Single-cell transcriptomic analysis of allergen-specific T cells in allergy and asthma.”](#) was supported by the National Institutes of Health (grants U19AI100275, U19AI135731, R01HL114093, S10RR027366 and S10 RR027366) and the William K. Bowes Jr. Foundation

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