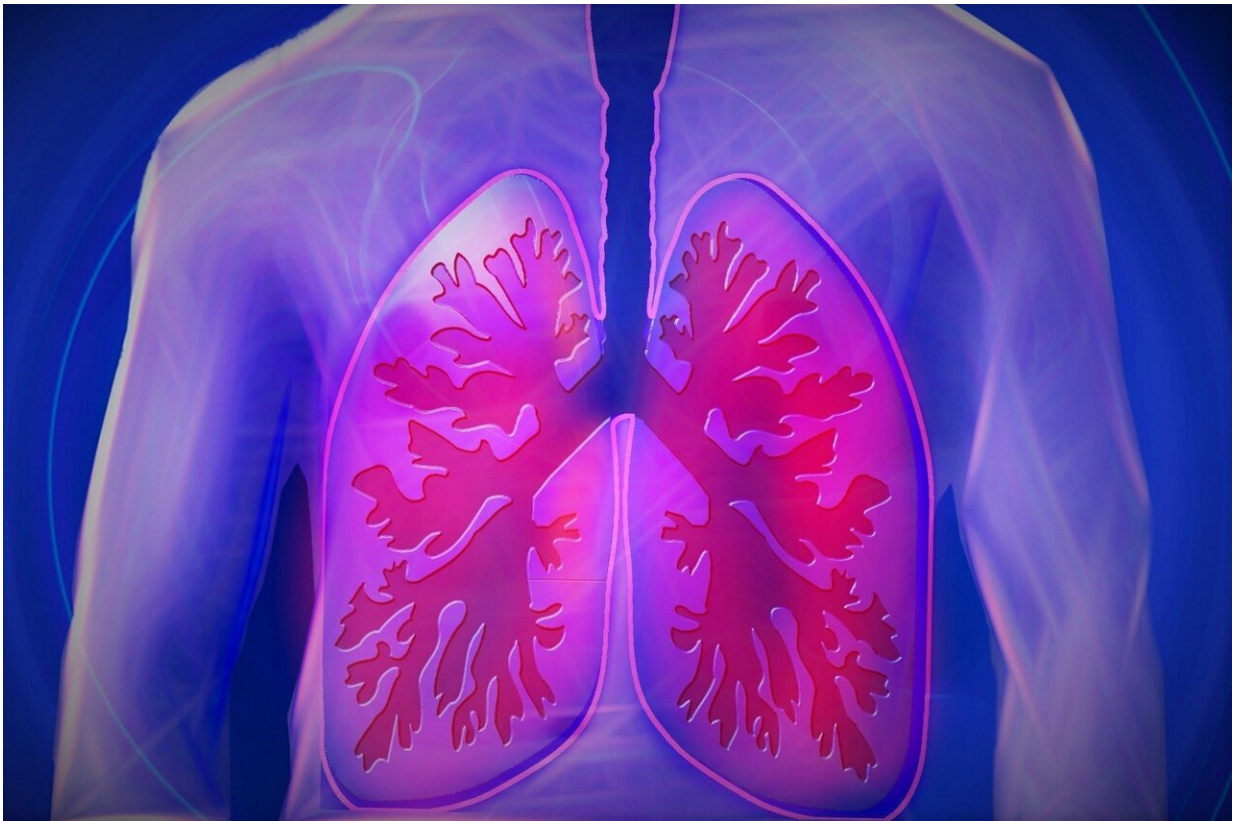


# Researchers identify immune profile for lung disease caused by allergic reaction

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Fibrotic hypersensitivity pneumonitis is a chronic and progressive interstitial lung disease, caused by an immune response to inhaled foreign antigens or allergens. Researchers from Yale's Section of

Pulmonary, Critical Care and Sleep Medicine have used single-cell sequencing technology to provide the first high-resolution atlas of this disease, revealing a previously unrecognized immune signature.

Their [findings](#) were published in the *American Journal of Respiratory and Critical Care Medicine*.

Fibrotic hypersensitivity pneumonitis belongs to a category of diseases known as pulmonary fibrosis, which is characterized by inflammation and irreversible scarring in the lungs. Other diseases under this umbrella include idiopathic pulmonary fibrosis, which is when scarring occurs in the lungs for an unknown reason.

Clinically, fibrotic hypersensitivity pneumonitis and idiopathic pulmonary fibrosis are hard to distinguish. "Patients with these diseases can present very similarly," says study lead author Amy Zhao, an MD/Ph.D. (genetics) student in the Kaminski lab at Yale.

"They may have similar symptoms and radiographic imaging, so patients will sometimes have to undergo further workup using invasive biopsies, and therapeutic decisions may be delayed."

Utilizing single-cell sequencing, a technology that allows measuring of all the genes expressed in every cell in a sample, Zhao and the Kaminski lab team analyzed over 500,000 peripheral blood [mononuclear cells](#) in patients with both diseases, as well as healthy controls.

In the blood of patients with fibrotic hypersensitivity pneumonitis, they identified previously unreported populations of immune cells with the capacity to kill other cells, known as cytotoxic T cells.

These cells carried a specific subpopulation of granzymes, enzymes that cause [cell death](#) and were relatively restricted to patients with fibrotic

hypersensitivity pneumonitis. Additionally, the team identified immune changes common to both ailments, including elevated classical monocytes in the blood.

"These findings may be helpful in the future for guiding diagnosis," says Zhao. "For example, if a patient has elevated levels of cytotoxic T cells, it suggests more likely that they have fibrotic hypersensitivity pneumonitis over idiopathic pulmonary fibrosis, but of course, more studies are required."

While there are currently two FDA-approved drugs and multiple other therapeutic trials for idiopathic [pulmonary fibrosis](#), [treatment options](#) for fibrotic hypersensitivity pneumonitis are dramatically understudied.

The principal investigator of this study, Naftali Kaminski, MD, Boehringer-Ingelheim Pharmaceuticals Professor of Medicine (pulmonary) and section chief of pulmonary, [critical care](#), and [sleep medicine](#), hopes that this study will spark specific therapeutic interventions for fibrotic hypersensitivity pneumonitis.

"There are very few [clinical trials](#) directly focused on fibrotic [hypersensitivity](#) pneumonitis," says Kaminski.

"Our current treatment paradigm involves antigen avoidance and immunosuppression, which are helpful during the acute or non-fibrotic phase, but inadequate during the fibrotic phase.

"Since immunity is still active during this phase, it's unlikely that only anti-fibrotics will help. By studying the immune system in these patients, we could develop novel targets that potentially limit the immune system from actively participating in lung scarring and fibrosis."

The researchers in this study used samples from cohorts of individuals

located in New Haven, Chicago, and Mexico. While they found significant shared immune responses across all these regions, as reported here, they also identified key differences, such as a specific T cell population found only in the patients from Mexico.

"This is among the first single cell sequencing studies that includes populations that are Latin American and that analyzes populations from different parts of the world," says Kaminski.

"The fact that we found similar findings between the groups is very reassuring. The fact that we also found findings specific to certain groups should encourage us to make sure that the populations we study are as diverse as possible."

**More information:** Amy Y Zhao et al, Single Cell Analysis Reveals Novel Immune Perturbations in Fibrotic Hypersensitivity Pneumonitis, *American Journal of Respiratory and Critical Care Medicine* (2024).  
[DOI: 10.1164/rccm.202401-0078OC](https://doi.org/10.1164/rccm.202401-0078OC)

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