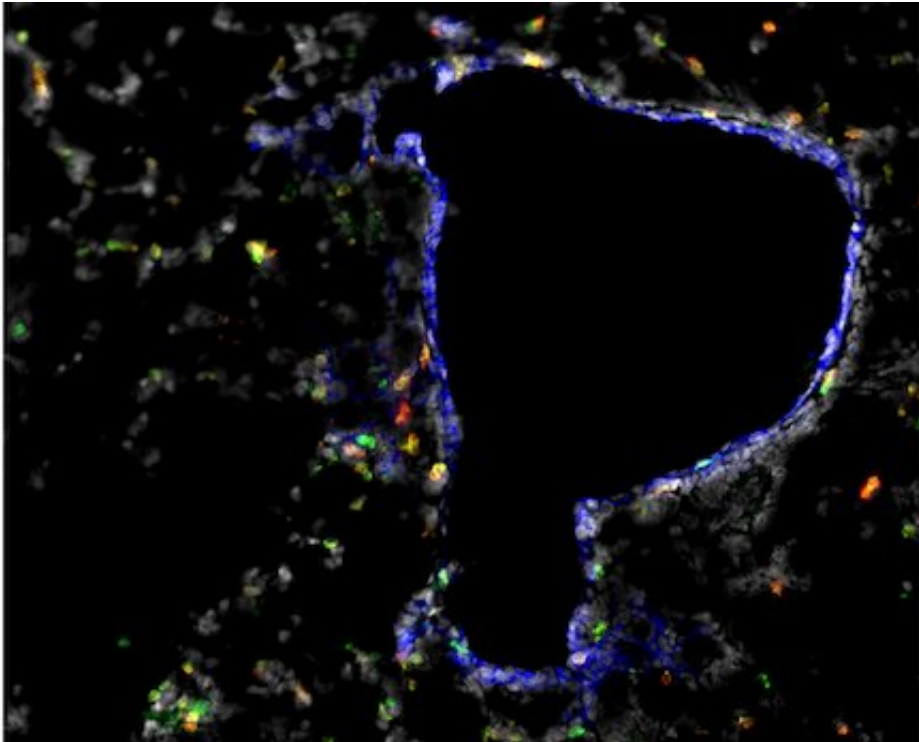


# Immunologists identify T cell homing beacons for lungs

September 27 2019, by Quinn Eastman

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T cells in mouse lung, courtesy of Alex Wein. Blue represents respiratory epithelium (EpCAM), while various T cells stain red, yellow or green. Credit: Emory University

Scientists have identified a pair of molecules critical for T cells, part of the immune system, to travel to and populate the lungs. A potential application could be strengthening vaccines against respiratory pathogens such as influenza.

The findings were published online Thursday, September 26 in *Journal of Experimental Medicine*.

Much research on immunity to influenza virus focuses on antibodies, infection- or vaccine-induced proteins in the blood that can smother viruses. But CD8 T [cells](#), which survey other cells for signs of viral infection and kill infected cells, are an important arm of our defenses too. The epitopes—or bits of viral protein—they recognize generally do not change from year to year.

Researchers led by Jacob Kohlmeier, Ph.D., at Emory University School of Medicine wanted to learn more about what's needed to get CD8 T cells into the lungs, since the lungs will often contain the first cells incoming virus will have a chance to infect. However, T cells don't stick around in the lungs for extended amounts of time.

"The airways are a unique environment in the body," says Alex Wein, a MD/Ph.D. student who trained in Kohlmeier's lab. "They're high in oxygen but low in nutrients. Unlike other tissues, when T cells enter the airways, it's a one-way trip and they have a half-life of a few weeks, so they must be continually repopulated."

Wein, his fellow MD/Ph.D. Sean McMaster, now at Boston Consulting Group, and Shiki Takamura at Kindai University are co-first authors of the paper. Kohlmeier is assistant professor of microbiology and immunology and part of the Emory-UGA Center of Excellence for Influenza Research and Surveillance.

The researchers showed that two molecules, called CXCR6 and CXCL16, are needed for CD8 T cells to reach the airways in mice. CXCR6 is found on T cells and CXCL16 is produced by the epithelial cells lining the airways of the lungs.

Other molecules necessary for T cells to home to the intestines or the skin were already known. The lungs have been more difficult to study because of how many blood vessels run through them. Recently, scientists have been able to discern two distinct populations of [lung T cells](#), present in the interstitium—between the lung [epithelial cells](#) and blood vessels—and others in the blood.

CXCR6 is a homing beacon that allows T cells to travel through the lung interstitium and into the airways.

"They might find their way to the right place anyway, but with the homing beacon, they get there faster and more reliably," Wein says. "Once they are there, they don't need it anymore."

Wein says that knowledge of CXCR6 and CXCL16 will be useful in designing adjuvants, or vaccine additives, which could allow recruitment of CD8 T cells into the airways. Current vaccines do not instruct the CD8 T cells to go to the airways; these cells are only present after a natural infection.

"If we can get long-lived T cells into the lungs of people that recognize conserved epitopes of influenza virus, they will get infected but have decreased symptoms or even be asymptomatic," Wein says.

Most of the experiments used mice, but the researchers did show that CXCR6 was abundant on CD8 T cells in the lungs of humans as well. CXCL16 is also made by the [airway epithelium](#) in humans.

**More information:** Alexander N. Wein et al. CXCR6 regulates localization of tissue-resident memory CD8 T cells to the airways, *The Journal of Experimental Medicine* (2019). [DOI: 10.1084/jem.20181308](https://doi.org/10.1084/jem.20181308)

Provided by Emory University

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