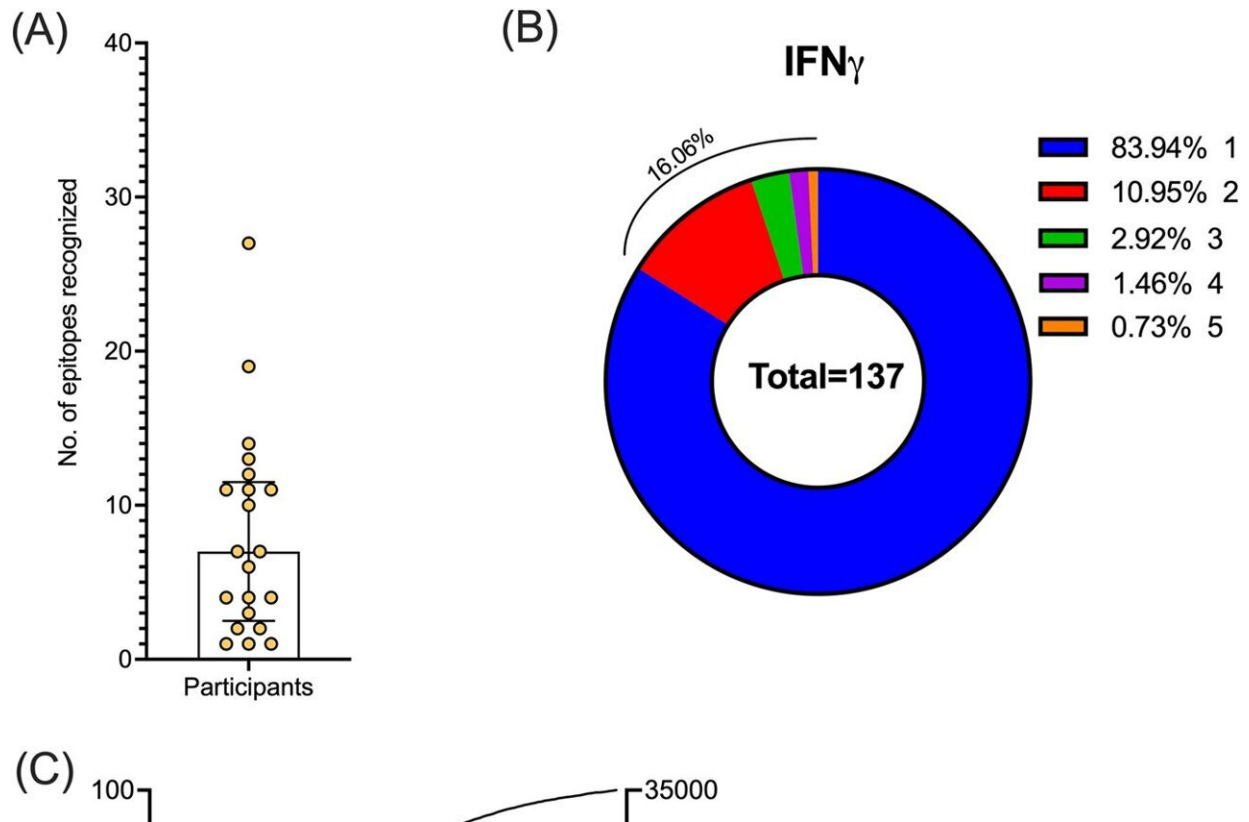


# Examining how T cells combat tuberculosis

February 6 2024



Breadth and dominance of epitopes in mid-treatment ATB participants. A Number of epitopes recognized by each participant. Each dot is one participant,  $n = 21$ ; median  $\pm$  interquartile range is shown. B Distribution of recognized epitopes by the number of participants recognizing each epitope. C Epitopes ranked based on the magnitude of response (solid line - % of total response, dotted line – total spot forming cells (SFC)). Black dotted lines indicate the top 55 epitopes. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-45058-9

La Jolla Institute for Immunology (LJI) is working to guide the development of new tuberculosis vaccines and drug therapies. Now, a team of LJI scientists has uncovered important clues to how human T cells combat *Mycobacterium tuberculosis*, the bacterium that causes TB. Their findings were published recently in [\*Nature Communications\*](#).

"This research gives us a better understanding of T cell responses to different stages in tuberculosis infection and helps us figure out if there are additional diagnostic targets, vaccine targets, or drug candidates to help people with the disease," says LJI Research Assistant Professor Cecilia Lindestam Arlehamn, Ph.D., who led the new research in collaboration with LJI Professors Bjoern Peters, Ph.D., and Alessandro Sette, Dr.Biol.Sci.

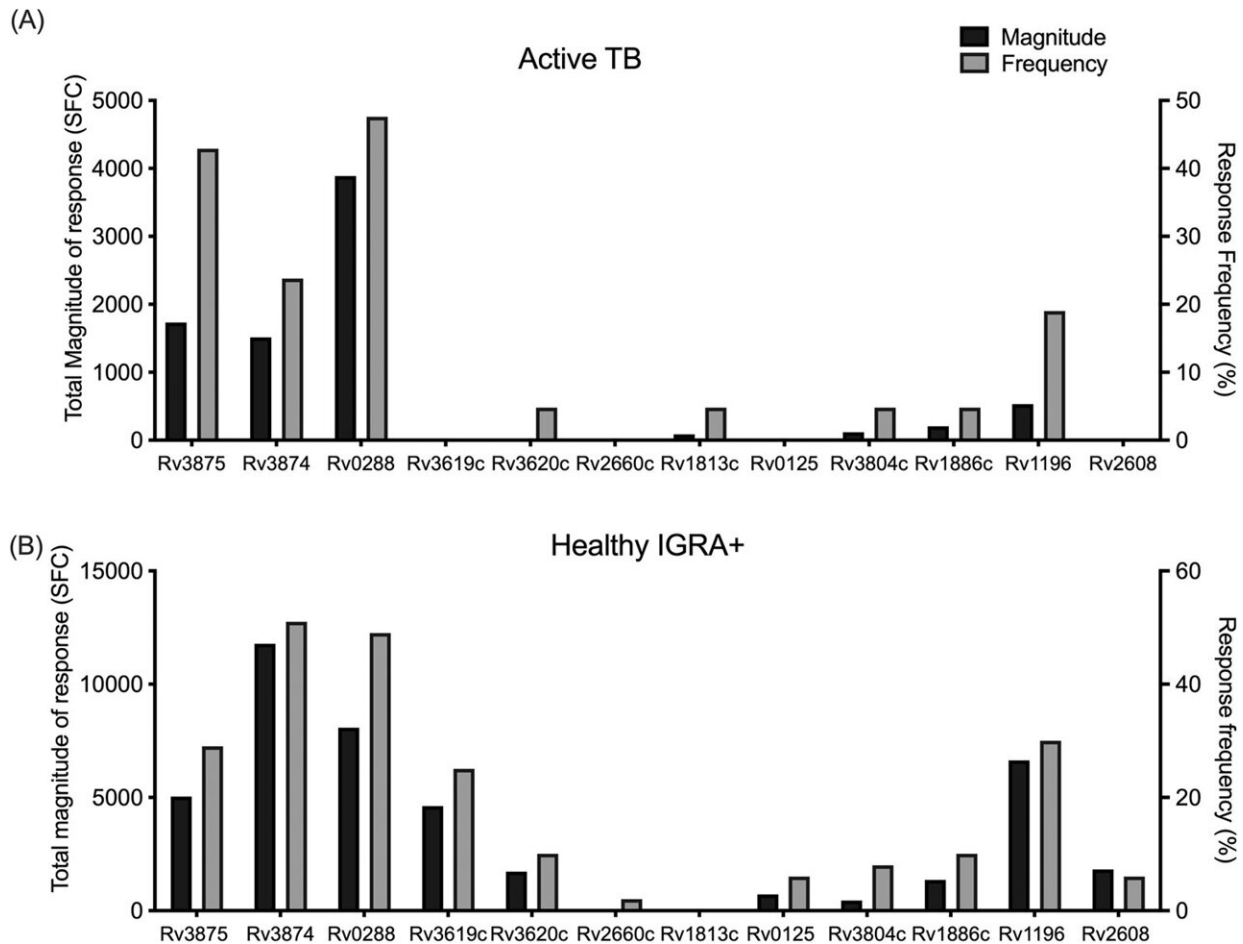
## **The urgent need for TB research**

According to the World Health Organization, more than 1.3 million people died of TB in 2022, making it the second-leading infectious cause-of-death after COVID-19. "TB is a huge problem in many countries," says Lindestam Arlehamn.

Currently, a vaccine called bacille Calmette-Guerin (BCG) protects against some severe cases of TB. Unfortunately, BCG doesn't consistently prevent cases of pulmonary TB, which can also be deadly. Although there are drug treatments for TB, more and more cases around the world have proven drug-resistant.

To help stop TB, Lindestam Arlehamn and her colleagues are learning from T cells. T cells are critical for stopping infections from spreading in the body. Instead of targeting an entire pathogen, T cells look for specific markers, called peptide sequences, that belong to the pathogen. When a T cell recognizes a certain part of a pathogen's peptide sequence, scientists call that area an "epitope."

Uncovering T-cell epitopes gives scientists vital information on how vaccines and drug treatments might take aim at the same epitopes to stop a pathogen.



Hierarchy in T cell reactivity against TB vaccine and IGRA antigens. Magnitude of response, expressed as the total magnitude of response (black bars, left y-axis) or frequency of participants responding (gray bars, right y-axis), among the participants. **A** ATB,  $n = 21$ . **B** Healthy IGRA + ,  $n = 63$ , for comparison purposes. Rv number for each antigen are indicated on the x-axis. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-45058-9

## **T cells take aim at a range of TB epitopes**

For the new study, the researchers worked with samples from patients who were mid-treatment for active TB. These samples came from study participants in Peru, Sri Lanka, and Moldova. By looking at T cells in patients from three different continents, the researchers hoped to capture a wide diversity of genetics—and [environmental factors](#)—that can affect immune system activity.

In their analysis, the LJI team uncovered 137 unique T-cell epitopes. They found that 16 percent of these epitopes were targeted by T cells found in two or more patients. The immune system appeared to be working hard to zoom in on these epitopes.

Going forward, Lindestam Arlehamn's laboratory will investigate which of these epitopes may be promising targets for future TB vaccines and drug therapies.

## **A step toward better diagnostics**

The new study is also a step toward catching TB cases before they turn deadly.

Because *Mycobacterium tuberculosis* is an airborne bacteria, a person can be exposed without ever realizing it. Once exposed, many people go months or years without any symptoms. This inactive, or "latent," TB can turn into active TB if a person's immune system weakens, for example, during pregnancy or due to an infection such as HIV.

For the new study, the researchers also compared samples from active TB patients to healthy individuals. The scientists uncovered key differences in T-cell reactivity between the two groups. "For the first time, we could distinguish people with active TB versus those that have

been exposed to TB—or unexposed individuals," says Lindestam Arlehamn.

Lindestam Arlehamn says it may be possible to develop diagnostics that detect this tell-tale T cell reactivity that marks a person's shift from latent to active TB. "Can we use this peptide pool to look for high-risk individuals and try and follow them over time?" she asks.

**More information:** Sudhasini Panda et al, Identification of differentially recognized T cell epitopes in the spectrum of tuberculosis infection, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-45058-9](https://doi.org/10.1038/s41467-024-45058-9)

Provided by La Jolla Institute for Immunology

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