

Genomic study reveals signs of TB adaptation in ancient Andeans

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People have inhabited the Andes mountains of South America for more than 9,000 years, adapting to the scarce oxygen available at high altitudes, along with cold temperatures and intense ultraviolet radiation.

A new genomic study suggests that Indigenous populations in present-day Ecuador also adapted to the tuberculosis bacterium, thousands of years before the arrival of Europeans.

The journal *iScience* published the findings, led by scientists at Emory University.

"We found that selection for genes involved in TB-response pathways started to uptick a little over 3,000 years ago," says Sophie Joseph, first author of the paper and an Emory graduate student in anthropology.

"That's an interesting time because it was when agriculture began proliferating in the region. The development of agriculture leads to more densely populated societies that are better at spreading a respiratory pathogen like TB."

The investigators had originally set out to investigate how the Indigenous people of Ecuador adapted to living at high altitude.

"We were surprised to find that the strongest genetic signals of positive selection were not associated with high altitude but for the [immune response](#) to tuberculosis," says John Lindo, Emory assistant professor of anthropology and senior author of the study. "Our results bring up more questions regarding the prevalence of tuberculosis in the Andes prior to European contact."

The Lindo lab specializes in mapping little-explored human lineages of the Americas.

Previously published research found evidence of the [tuberculosis bacterium](#) in the skeletal material of 1,400-year-old Andean mummies, contradicting some theories that TB did not exist in South America until the arrival of Europeans 500 years ago.

The current paper provides the first evidence for a human immune-system response to TB in ancient Andeans and gives clues to when and how their genomes may have adapted to that exposure.

"Human-pathogen co-evolution is an understudied area that has a huge bearing on modern-day public health," Joseph says. "Understanding how pathogens and humans have been linked and affecting each other over time may give insights into novel treatments for any number of infectious diseases."

Co-authors of the paper include scientists at Central University of Ecuador, Technical University of Manabi in Ecuador, University of Pavia in Italy, University of Iowa and Florida Atlantic University.

The researchers sequenced whole genomes using [blood samples](#) from 15 present-day Indigenous individuals living at altitudes above 2,500 meters in several different Ecuadorian provinces. They performed a series of scans to look for signatures of positive selection for genes in their ancestral past.

"Computational techniques for sequencing genomes and modeling ancestral selection keep improving," Joseph says. "The genomes of people living today give us a window into the past."

Among the strongest signals detected were for biomarkers that are switched on in modern humans during an active TB infection. The researchers modeled the timing of selection for several of the genes involved in the TB-response pathways.

Although they were not as strong as for exposure to TB, some signals were also detected for biomarkers related to adaptation to hypoxia, or low levels of oxygen in the blood that result from living at high altitude.

Previous research has revealed stark differences in how [high-altitude](#) populations in Tibet, Ethiopia and the Peruvian Andes adapted to hypoxia.

"For the Ecuadorean samples, we did see a couple of overlaps with studies from the Peruvian Andes in the overarching genes involved in the selection for hypoxia, although the variants were slightly different," Joseph says. "To me, that suggests that there may have been independent adaptations within even small populations, at the community level. It shows the robustness of the genome to solve adaptive problems through different pathways."

Joseph plans a career focused on mapping ancestral data for Indigenous populations from the Americas.

"South America has far fewer genomic studies and publications compared to Europe and I'd like to help close that gap," she says.

"I want to understand human evolution and health from an integrated biological perspective," Joseph adds. "The genome can reveal many fascinating things and yet it is just one aspect of a human being. You also have to consider the environment and social-cultural aspects."

More information: Sophie K. Joseph et al, Genomic evidence for adaptation to tuberculosis in the Andes before European contact, *iScience* (2023). [DOI: 10.1016/j.isci.2023.106034](https://doi.org/10.1016/j.isci.2023.106034)

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