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[Sonia Fernandez](#)

Microbiome study reveals ancient gut connections between Africa and South America

What do the Tsimané of lowland Bolivia have in common with the Hadza of Tanzania? Aside from their mostly nonindustrial lifestyles and the ocean between them for millennia, the two populations have highly diverse and strikingly similar gut microbiomes, researchers at UC Santa Barbara and Stanford University have found

“We’re learning yet another way that urbanization and industrialization have rapidly impacted our bodies and our health,” said UCSB anthropologist [Michael Gurven](#).

The researchers’ study is published in the journal [Nature](#).

Ancient traveling companions

The gut microbiome has garnered a lot of attention in recent decades for the many beneficial functions it performs, including the digestion of fibrous food, making vitamins and training our immune systems. Indeed, evidence shows that lifestyle impacts the microbiome’s composition, which in turn can affect health. People living in industrialized countries show a profound loss of microbiome diversity compared with people living nonindustrialized lifestyles. They also suffer from autoimmune diseases, Type 2 diabetes, obesity and other chronic conditions that are rare among nonindustrialized groups.

For Gurven, a distinguished professor of anthropology and co-director of the Tsimané Health and Life History Project, the difference in gut biodiversity in rural-living Tsimané versus that of typical city dwellers is intriguing. In previous work, Gurven and collaborators found that environmental and lifestyle factors seem to protect Tsimané from heart disease and other chronic conditions that accompany industrialized lifestyles, but could the diversity of the gut microbiome also play a role? More specifically, could microbiome loss — as is the case with industrialized populations — contribute to common chronic conditions, such as autoimmune diseases or obesity?

To address that question, the researchers needed to first understand the evolution of the human gut microbiome and its diversity going back millennia. Gaining insight into which, if any, long-term residents of the microbiome co-evolved with humans could inform future investigation of how the loss of microbial diversity through urbanization impacts human biology.

For their study, the researchers conducted the first-ever deep comparison of the microbiomes of the Hadza in Tanzania — one of the world's few remaining hunter-gatherer groups — and the Tsimané, Indigenous forager-farmers living in the Bolivian Amazon whose lifestyle has had comparatively limited exposure to industrialization. Although the ancestral human populations that ultimately gave rise to the two groups became geographically separated tens of thousands of years ago, the Hadza and Tsimané surprisingly share over 1,200 bodily bacterial species and nearly 90% of species identified in the highly diverse Tsimané microbiomes. Most of those species — about 60% — are rare or completely absent in the microbiomes of industrialized populations.

Using several complementary population genetics analysis techniques, the researchers estimated when microbial strains separated. For many species, those estimates correspond to the timeframe of major prehistoric human migrations out of Africa and into the Americas. The ultimate takeaway: many microbial lineages in these contemporary populations have deep evolutionary roots extending back through ancient human migrations.

“Our study establishes that the hundreds of bacterial species that are rare or missing in industrialized microbiomes were ancient companions of ours as we migrated around the globe, likely passed from generation to generation for

millennia,” said senior author [Justin Sonnenburg](#), a Stanford professor of microbiology and immunology. “This long-term association has implications for how such recent biodiversity loss in our microbiome may impact our biology and thus our health.”

Deep genomic analysis

The researchers used deep metagenomic sequencing, a method that characterizes the microbes present in a sample by reading out all the letters of the DNA building blocks. Millions of small sequences of DNA are generated with overlapping stretches of letters indicating where the small sequences match up into longer sequences. Those long sequences are then compared with databases of microbial genomes to identify the detected organism.

The Tsimané Health and Life History Project team collected voluntary stool samples from the Tsimané. Sonnenburg and colleagues previously completed a metagenomic sequencing on Hadza samples showing, among other findings, that the average Hadza individual has about 750 species in their microbiome, while the average Californian has a mere 250. For the new study, the researchers did the first deep sequencing of the Tsimané samples, which had [previously](#) only been sequenced at low resolution.

The sequencing efforts enabled the researchers to build a comprehensive census of the microbes in the respective microbiomes, including hard-to-capture, low-abundance species. Overall, the sampled Tsimané individuals hosted a combined total of about 1,400 different species; remarkably, the Tsimané shared a total of 1,231 of these species (~90%) with the Hadza, according to the new analysis.

“We were really surprised to see that the vast majority of the species in the Tsimané’s microbiome correspond with the Hadza’s,” Sonnenburg said.

Different lifestyles, similar results

Some of that surprise stems from the considerably different diets between the two groups. The Hadza hunt meat from mammals including impala and kudu, along with birds and fish, and forage for fruits and vegetables, including tubers and berries. By contrast, the Tsimané grow much of their food and [consume](#) high levels of fiber

through plantains, rice, manioc root and corn, along with lean meat from fish, peccary and other forest animals.

Additionally, the two groups have also been separated for tens of thousands of years. Despite this geographic and lifestyle separation, the two microbiomes showed remarkable overlap at the species level.

“That made us wonder if there really is a core set of bacterial and other species that traveled with the ancestors of the Tsimané as they migrated around the globe,” said Stanford’s [Benjamin Good](#), Ph.D., the study’s senior co-author and an assistant professor of applied physics who specializes in investigating evolutionary dynamics and population genetics of the human gut microbiome.

“Could these bugs have been in continual interaction with us since long before the ancestors of today’s Hadza and Tsimané became geographically separated?” Sonnenburg asked. “To answer that, we turned to Ben’s team, and what they found blew our minds.”

An interwoven biology goes way back

Unpacking the evolutionary history of a microbiome overall has proven daunting given complexities posed by how quickly microbes evolve and the changes a given person’s microbiome can undergo from season to season, or based on other aspects of food availability.

Good’s group sought to get around these issues. Bacteria complicate evolutionary reconstruction because they not only inherit DNA from their ancestors but also frequently exchange DNA with other strains in a process known as horizontal gene transfer. The researchers therefore looked for several independent genomic signatures to distinguish deep shared ancestry from more recent microbial exchange. Looking at mutation rates in vertically inherited DNA also helped estimate when species diverged from a common ancestor because mutations accumulate at a steady pace, like ticks of a clock.

That analysis squarely indicated that many of the shared bacterial species between the nonindustrialized groups’ microbiomes have evolutionary histories that trace back over thousands of years. These detailed analyses of genetic isolation of strains produced time estimates consistent with the timing of major human migrations.

“What’s amazing is that Tsimané and Hadza share so many of the same endangered bacterial species in their guts, not because they both live in rural areas with low access to antibiotics — but because they’ve been carrying these same species for hundreds of generations,” Gurven explained. “The analysis shows strong evidence that their ancestors, and presumably all of us, had these same bacteria long ago.”

If humans interacted with many of these organisms for tens of thousands of years, the researchers said, what happens when industrialization eliminates a large portion of them over just a few generations? Previous work in the field links changes in microbiomes to many disease states. Dramatic changes to our resident microbial populations — attributed to antibiotic exposure; low-fiber, high-fat and high-sugar diets of processed food; highly sanitized living conditions; and other factors — could be incompatible with our human-genome encoded biology. The biological consequences of this recent biodiversity loss are an important next step for study.

Some of those differences may be revealed not just by comparing populations like the Tsimané with the U.S., but by examining all the changes affecting Tsimané lives over the past couple decades. “With rapid changes in diet and access to medicines, Tsimané microbiomes could soon lose their diversity,” Gurven said, “and the impacts of that loss could harm their immunity and health.”

Media Contact

Sonia Fernandez

Senior Science Writer

(805) 893-4765

sonia.fernandez@ucsb.edu

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