Cecil Lewis uses a pipette and pH indicator dyes to purify DNA extracts in his Norman campus laboratory. The anthropological geneticist employs the latest scientific advances to study the human microbiome.

Travis Caperton

The Secret World of Microbiomes

OU anthropologists track the microbes of our ancestors to find cures for diseases of today.

BY CHIP MINTY

Two University of Oklahoma researchers are using technology to cast an illuminating light on the past, hoping to find clues that could help cure some of the most threatening diseases in the world today.

Cecil Lewis and Christina Warinner are OU anthropologists, so they are in the business of studying ancient life. But what sets these scientists apart is their acute interest in using what they learn to improve the future.

They are working in an expanded world of anthropology that includes DNA, RNA, genetic sequencers and grants from the National Institutes of Health. A term for what they do is "anthropological genetics," which means they venture far from the realm of Indiana Jones into the technological frontiers of biochemistry.

Remember the Human Genome Project? Lewis knows some of the people who helped unravel the genetic code of an entire human chromosome, including OU's Bruce Roe, a George Lynn Cross Research Professor of Chemistry and Biochemistry.

Roe is now retired, but Lewis and Warinner, co-founders of OU's Molecular Anthropology and Microbiome Research Laboratories, are building on the genome project's accomplishments. They are using technology Roe and his colleagues developed to sequence DNA, but instead of human genes, they study the microbes that live on us and in us.

Lewis was part of the Human Microbiome Project, which identified and characterized the microorganisms associated with the human body. His work came on the heels of Roe's scientific milestone, and the project has helped expand the

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Christina Warinner presents a TED Talk on how plaque extracted from ancient skeletons and mummies is helping scientists understand changes in human pathogens over thousands of years.

study of anthropological genetics to include the human microbiome. By studying humans at gut level, scientists believe they may be able to answer fundamental questions about human health, such as the rapidly increasing rate of autoimmune diseases like diabetes, rheumatoid arthritis and Crohn's disease.

The human microbiome consists of a wide variety of bacteria, viruses and other microbes that live in and on human bodies. The heaviest accumulations are in the mouth and the gut, and they serve symbiotic functions critical to survival, Lewis says.

Typically, a person contains more than twice as many microorganisms as actual human cells. The number exceeds 40 trillion, and they combine to weigh about three pounds, or as much as the human brain, Lewis says. Microbes are so vital to our survival that Lewis likens them to another vital organ, such as a liver or heart.

"They are important to life," he says. "Without them, you would be dead."

But he and research partner Warinner are not focusing on the microbial colonies inhabiting people in shopping malls and fast-food restaurants. Instead, these anthropologists are focused on people living ancient lifestyles in fields and forests, hunting and gathering just as humans did 10,000 years ago.

Their subjects include people currently living traditional lifestyles in some of the world's most remote regions, along with the microbiomes of ancient people who lived similar lives hundreds and even thousands of years ago. Warinner's work has focused on collecting DNA from prehistoric people in Europe, North America, South America and Asia, including research on the earliest inhabitants of the Himalayas, which was featured in the NOVA documentary, *Secrets of the Sky Tombs*, broadcast on PBS. The researchers are comparing the microorganisms found in ancient peoples and remote populations to those of contemporary urban dwellers to see if something in the gut got lost along the road to industrialization.

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If their hypothesis is proven, they could find clues that might lead to greater health and wellness for millions of people suffering from chronic diseases.

Clouds of condensation roll over Cecil Lewis as he opens an ultra-low temperature freezer, where such biological samples as DNA, blood and cheek swabs are kept at minus-80 degrees for future research.

Photo provided

Christina Warinner's collaboration with Cecil Lewis is building on the success of the Human Genome Project to identify and characterize human microorganisms.

Photo provided

Christina Warinner, fourth from left, with the 2012 field crew who excavated the highest-known burial sites in the world. The team's research in Nepal was featured in the recent *NOVA* documentary, *Secrets of the Sky Tombs,* on PBS.

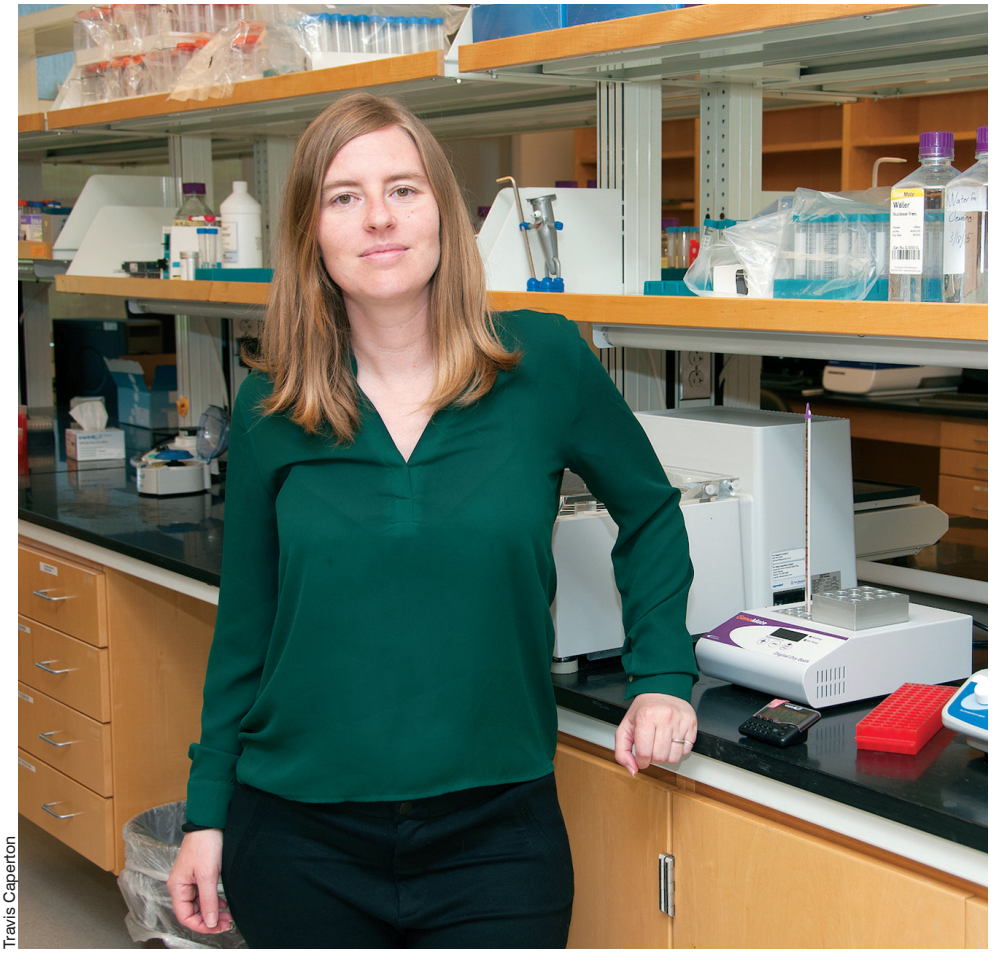
The stakes are high. If their hypothesis is proven, they could find clues that might lead to greater health and wellness for millions of people suffering from chronic diseases. Growing volumes of information about the human microbiome today have led to new questions pertaining to microbiomes of the past.

Has the human microbiome always looked like it does today, or has it changed as humans have evolved from hunters and gatherers to farming cultures and, finally, to industrial societies? Have the changes in living conditions, food and behavior made a difference? If so, what kind of impact has that had on health?

Those are reasonable questions, Warinner says, considering how different the modern world is from what it was thousands of years ago. She and Lewis suspect that antibiotics, chlorinated water, processed foods and other antiseptic measures taken to promote health have actually changed our microbiomes. Now, their lab is working to find evidence.

They think they may have found it among people living as traditional foragers and hunters in the remote African savannahs of Tanzania and in the Amazon forests of Venezuela. Hunter-gatherers from those populations have tremendous biome diversity when compared to their counterparts in the industrialized world, Warinner says.

Meanwhile, Lewis has found similar results by studying ancient people who lived in central Mexico 700 years ago. His study involved the analysis of DNA found in coprolites, a term anthropologists use for ancient feces. Lewis and Warinner are now carrying this work forward by studying additional ancient coprolite samples from around



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As co-founder of OU's Molecular Anthropology and Microbiome Research Laboratories, Christina Warinner is working to solve basic questions about the evolution of human health by studying microbes that live in and on our bodies.

the world, as well as calcified dental plaque, or tooth tartar. The study of ancient human feces and tooth tartar is opening the door to revelations that were beyond the reach of science a decade ago.

Though their work, Lewis and Warinner have identified a bacterium that appears to be prominent in the gastrointestinal tracts of traditional cultures and ancient humans, but nonexistent in modern Western society. The microbe is from the *Treponema* genus, and Lewis says it belongs to an evolutionary group of beneficial bacteria that assists in the conversion of fiber into energy. A byproduct of that process has anti-inflammatory properties.

Lewis wonders if the absence of those beneficial anti-inflammatory properties could help explain the increases in inflammatory diseases in the modern world. Could this or other microbes missing in the modern human microbiome be a factor in the proliferation of autoimmune diseases?

"It's a hypothesis that is very compelling, and I think we're onto something," Lewis says.

From their work, Lewis and his team know the *Treponema succinifaciens* bacterium was once part of the human microbiome, and now they want to know why it is gone. They also need to know what it is capable of, and if it truly can promote better health in industrialized populations.

Answers to those questions could lead to better health through the development of new probiotics and a more knowledgeable approach to antibiotics. In his search for potential solutions, Lewis says one thing is certain. Turning back the clock is not the answer.

"I'm not suggesting we get rid of chlorinated water and sanitized food, and I'm not saying to go back to the traditional lifestyle. But, if we can understand the traditional state, we can make the industrial lifestyle better," he says.

In their lab Lewis and Warinner are exploring the ancient microbiomes of the world to determine what was there in the beginning and what is missing today. The next challenge will be to understand why the missing microorganisms disappeared, to determine if they are beneficial, and, if so, to establish ways to reintroduce them into the microbiomes of present-day humans. If they could do that, they may be able to help thousands and perhaps millions of inflicted people fight their diseases, reduce their symptoms or avoid them altogether.

For this band of anthropological forerunners, that's a holy grail worth searching for.

Chip Minty is a Norman-based writer and the principal of Minty Communications, LLC.