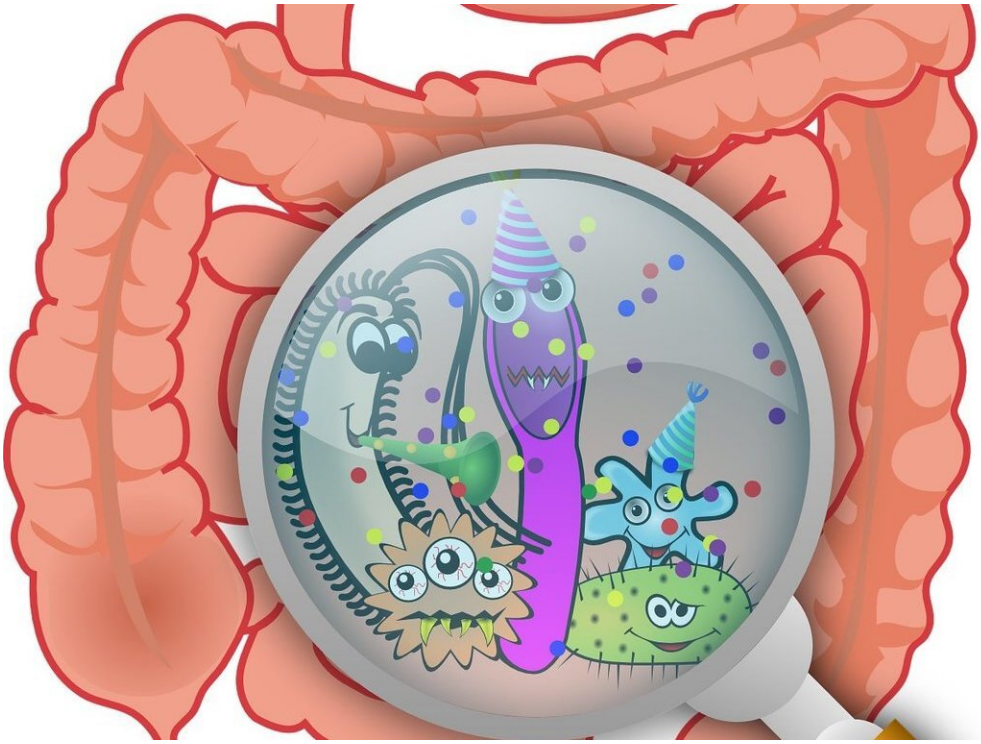
Each human gut has a viral 'fingerprint'

August 24 2020, by Emily Caldwell



Credit: CC0 Public Domain

Each person's gut virus composition is as unique as a fingerprint, according to the first study to assemble a comprehensive database of viral populations in the human digestive system.

An analysis of viruses in the guts of healthy Westerners also showed that dips and peaks in the diversity of virus types between childhood and old

age mirror bacterial changes over the course of the lifespan.

The Gut Virome Database developed by Ohio State University scientists identifies 33,242 unique viral populations that are present in the human gut. (A collection of viruses like those in the human gut is called a virome.) This is not cause for alarm: Most viruses don't cause disease.

In fact, the more scientists learn about viruses, the more they see them as part of the human ecosystem—suggesting viruses have potential to represent a new class of drugs that could fight disease-causing bacteria, especially those resistant to antibiotics. Better knowledge of viruses in the gut environment could even improve understanding of the gastrointestinal symptoms experienced by some of the sickest COVID-19 patients.

The researchers plan to update the open-access database on a regular basis.

"We've established a robust starting point to see what the virome looks like in humans," said study co-author Olivier Zablocki, a postdoctoral researcher in microbiology at Ohio State. "If we can characterize the viruses that are keeping us healthy, we might be able to harness that information to design future therapeutics for pathogens that can't otherwise be treated with drugs."

The study is published today (Aug. 24) in the journal *Cell Host & Microbe*.

Talk of the good and bad bacteria in the gut microbiome is commonplace these days, but viruses in the gut—and everywhere—are hard to detect because their genomes don't contain a common signature gene sequence that bacteria genomes do. So much of the vast sequence space of viruses remains unexplored that it is often referred to as "dark

matter."

For this work, the researchers started with data from 32 studies over about a decade that had looked at gut viruses in a total of 1,986 healthy and sick people in 16 countries. Using techniques to detect virus genomes, the team identified more than 33,000 different viral populations.

"We used machine learning on known viruses to help us identify the unknown viruses," said first author Ann Gregory, who completed this work while she was a graduate student at Ohio State. "We were interested in how many types of viruses we could see in the gut, and we determined that by how many types of genomes we could see since we couldn't visually see the viruses."

Their analysis confirmed findings from smaller studies suggesting that though a few viral populations were shared within a subset of people, there is no core group of gut viruses common to all humans.

A few trends were identified, however. In healthy Western individuals, age influences the diversity of viruses in the gut, which increases significantly from childhood to adulthood, and then decreases after age 65. The pattern matches what is known about ebbs and flows of gut bacterial diversity with one exception: Infant guts with underdeveloped immune systems are teeming with a range of virus types, but few bacteria varieties.

People living in non-Western countries had higher gut virus diversity than Westerners. Gregory said other research has shown that non-Western individuals who move to the United States or another Western country lose that microbiome diversity, suggesting diet and environment drive virome differences. (For example, the scientists found some intact plant viruses in the gut—the only way for them to get there is through

the diet.) Variations in viral diversity could also be seen in healthy versus sick participants in the 32 studies analyzed.

"A general rule of thumb for ecology is that higher diversity leads to a healthier ecosystem," Gregory said. "We know that more diversity of viruses and microbes is usually associated with a healthier individual. And we saw that healthier individuals tend to have a higher diversity of viruses, indicating that these viruses may be potentially doing something positive and having a beneficial role."

Almost all of the populations—97.7 percent—were phages, which are viruses that infect bacteria. Viruses have no function without a host—they drift in an environment until they infect another organism, taking advantage of its properties to make copies of themselves. The most-studied viruses kill their host cells, but scientists in the Ohio State lab in which Gregory and Zablocki worked have discovered more and more phage-type viruses that coexist with their host microbes and even produce genes that help the host cells compete and survive.

The leader of that lab, senior study author Matthew Sullivan, has his sights set on "phage therapy"—the 100-year-old idea of using phages to kill antibiotic-resistant pathogens or superbugs.

"Phages are part of a vast interconnected network of organisms that live with us and on us, and when broad-spectrum antibiotics are used to fight against infection, they also harm our natural microbiome," Sullivan said. "We are building out a toolkit to scale our understanding and capabilities to use phages to tune disturbed microbiomes back toward a healthy state.

"Importantly, such a therapeutic should impact not only our human microbiome, but also that in other animals, plants and engineered systems to fight pathogens and superbugs. They could also provide a foundation for something we might have to consider in the world's

oceans to combat climate change."

A professor of microbiology and civil, environmental and geodetic engineering, Sullivan has helped establish cross-disciplinary research collaborations at Ohio State. He recently founded and directs Ohio State's new Center of Microbiome Science and co-directs the Infectious Diseases Institute's Microbial Communities program.

Zablocki noted that there is still a lot to learn about the functions of viruses in the gut—both beneficial and harmful.

"I see it as the chicken and the egg," he said. "We see the disease and we see the community structure. Was it because of this community structure that the disease occurred, or is the disease causing the community structure that we see? This standardized dataset will enable us to pursue those questions."

More information: Ann C. Gregory et al, The Gut Virome Database Reveals Age-Dependent Patterns of Virome Diversity in the Human Gut, *Cell Host & Microbe* (2020). DOI: 10.1016/j.chom.2020.08.003

Provided by The Ohio State University