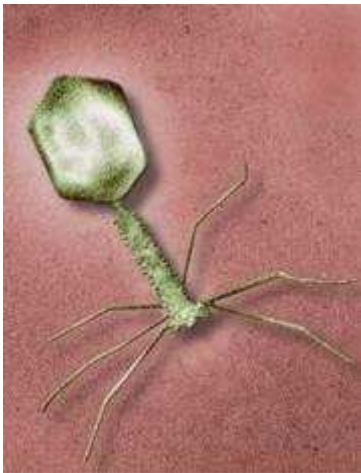


The gut's 'friendly' viruses revealed

DNA sequencing reveals a new world of bacterial viruses in our intestines.

Amy Maxmen



In the gut, viruses that normally prey on bacteria seem to live in harmony with them. *DR. HAROLD FISHER, VISUALS UNLIMITED /SCIENCE PHOTO LIBRARY*

In the latest exploration into the universe of organisms inhabiting our bodies, microbiologists have discovered new viral genes in faeces. They find that the composition of virus populations inhabiting the tail ends of healthy intestines (as represented in our stools) is unique to each individual and stable over time. Even identical twins — who share many of the same intestinal bacteria — differed in their gut's viral make-up.

More than 80% of the viral genetic sequences found, which included sequences characteristic of both animal and bacterial viruses, have never been reported previously. "This is a largely unexplored world," says Jeffrey Gordon at Washington University in St Louis, Missouri, and an author on the paper, which is published in *Nature* today¹. "We are truly distinct lifeforms — sums of microbial and human parts."

More than 10 trillion bacteria normally inhabit the gastrointestinal tract, where they synthesize essential amino acids and vitamins, produce anti-inflammatory factors and help break down starches, sugars and proteins that people could not otherwise digest. Within and among these bacteria live bacterial viruses, or bacteriophages, which affect bacterial numbers and behaviour as they either prey on bacteria or co-exist with them, shuttling genes from one bacterium to another.

This microscopic dynamic ecosystem affects our lives in ways we still do not fully understand. Indeed, the rise in the incidence of food allergies in Western societies

has led to hypotheses that extreme hygiene disrupts the ability of microbes to colonize human guts, resulting in a lack of tolerance to usually harmless foods.

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To explore this provocative hypothesis, researchers must first understand the complete composition of the microbial ecosystem of the healthy body. To this end, Gordon's group and others are beginning to catalogue the human 'microbiome', all the microorganisms living in the human body, using advanced DNA sequencing technologies. Until now, however, such attention has primarily focused on the bacteria rather than viruses.

"This is a wonderful study," says David Relman, a microbiologist at Stanford University in California, who is involved with the US National Institute of Health's Human Microbiome Project. "It could be that viruses are the real drivers of the system because of their ability to modify the bacteria that then modify the human host," he says. "So this study is in some ways looking into the genesis of the human body by seeing what viruses within it are up to."

Microbial truce

According to the new study, bacterial viruses in the terminal gut or colon seem to exist in a more stable state than do similar communities in the environment, such as in the oceans. Faeces from each individual — four pairs of identical twins and their mothers — carried a distinct viral community that varied by less than 5% over the course of a year. The bacterial viruses also appeared to mainly be lying low as 'prophages' rather than multiplying and killing the bacteria they infect.

"In oceans, the modality of viruses has tended to be predatory," comments Edward DeLong at the Massachusetts Institute of Technology in Cambridge. "Now the interesting thing here is that the system in the faecal microbiota seems to be driven by prophages, which tend to basically integrate their genetic material into the host genome and hide there — it's a much more stable situation."

"This kind of stability implies that there is a symbiosis between bacteria and viruses," comments Martin Blaser at New York University Medical Center. "This is different from a predator-prey, or an arms race, situation. This is a picture of a more settled existence, in which the different populations are working together."

The team found genes encoding proteins never detected before in bacterial viruses. When in bacteria, these proteins are part of pathways responsible for carbohydrate metabolism and amino-acid synthesis. Viruses carrying such genes might alter them and insert them into gut bacteria, potentially changing a person's metabolism.

Because human nutrition partly depends on the relationship between bacteria and their viruses, understanding the dynamics of that relationship might yield treatments for obesity, allergies and other maladies. "This human ecosystem is quite important because it determines what we can do and what we can eat," says DeLong. "That's why we should care about this."

1.

Reyes, A. *et al.* *Nature* **466**, 334-340 (2010).