



the organs and tissues. The digestive tract is also home to a vast colony of bacteria of all varieties, as well as the myriad viruses that prey upon them. Because the types of bacteria carried inside the body vary from person to person, so does this viral population, known as the virome.

By closely following and analyzing the virome of one individual over two-and-a-half years, researchers from the Perelman School of Medicine at the University of Pennsylvania, led by professor of Microbiology Frederic D. Bushman, Ph.D., have uncovered some important new insights on how a viral population can change and evolve – and why the virome of one person can vary so greatly from that of another. The evolution and variety of the virome can affect susceptibility and resistance to disease among individuals, along with variable effectiveness of drugs.

Their work was published in the *Proceedings of the National Academy of Sciences*.

Most of the virome consists of bacteriophages, viruses that infect [bacteria](#) rather than directly attacking their human hosts. However, the changes that bacteriophages wreak upon bacteria can also ultimately affect humans.

"Bacterial viruses are predators on bacteria, so they mold their populations," says Bushman. "Bacterial viruses also transport genes for toxins, [virulence factors](#) that modify the phenotype of their bacterial host." In this way, an innocent, benign bacterium living inside the body can be transformed by an invading virus into a dangerous threat.

At 16 time points over 884 days, Bushman and his team collected stool samples from a healthy male subject and extracted [viral particles](#) using several methods. They then isolated and analyzed DNA contigs (contiguous sequences) using ultra-deep [genome sequencing](#) .

"We assembled raw sequence data to yield complete and partial genomes and analyzed how they changed over two and a half years," Bushman explains. The result was the longest, most extensive picture of the workings of the human virome yet obtained.

The researchers found that while approximately 80 percent of the viral types identified remained mostly unchanged over the course of the study, certain viral species changed so substantially over time that, as Bushman notes, "You could say we observed speciation events."

This was particularly true in the Microviridae group, which are bacteriophages with single-stranded circular DNA genomes. Several genetic mechanisms drove the changes, including substitution of base chemicals; diversity-generating retroelements, in which reverse transcriptase enzymes introduce mutations into the genome; and CRISPRs (Clustered Regularly Interspaced Short Palindromic Repeats), in which pieces of the DNA sequences of bacteriophages are incorporated as spacers in the genomes of bacteria.

Such rapid evolution of the virome was perhaps the most surprising finding for the research team. Bushman notes that "different people have quite different bacteria in their guts, so the viral predators on those bacteria are also different. However, another reason people are so different from each other in terms of their virome, emphasized in this paper, is that some of the viruses, once inside a person, are changing really fast. So some of the viral community diversifies and becomes unique within each individual."

Since humans acquire the bacterial population—and its accompanying virome—after birth from food and other environmental factors, it's logical that the microbial population living within each of us would differ from person to person. But this work, say the researchers, demonstrates that another major explanatory factor is the constant

evolution of the virome within the body. That fact has important implications for the ways in which susceptibility and resistance to disease can differ among individuals, as well as the effectiveness of various drugs and other treatments.

Provided by University of Pennsylvania School of Medicine

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