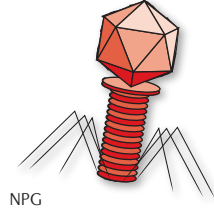
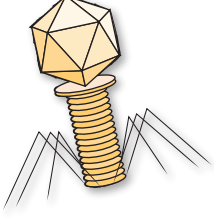
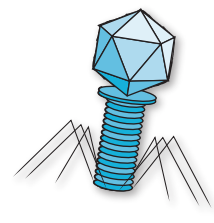
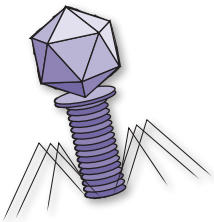
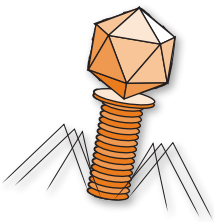
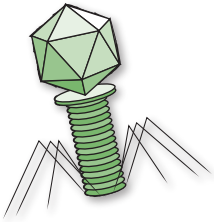


 VIRAL EVOLUTION

## Variation in the gut virome



NPG

The composition of the human gut virome shows substantial variation: 1 g of faeces contains more than  $10^9$  virions, and viral populations differ greatly between humans. Some of this variation has been linked to individual differences in bacterial colonization. Many members of the gut virome are phages, which often infect specific bacterial species and thus can be found only in humans that harbour these bacteria. A new study now finds that, in addition to the variability that depends on the presence of individual gut bacteria, the viral populations themselves undergo rapid evolution, giving rise to new phage species.

Previous studies of the gut virome focused on subjects with diseases, such as people infected with HIV, and identified many human viruses in the gut virome. The current study, however, followed a healthy adult male for 2.5 years by repeated sampling, purification of viral DNA and amplification of that DNA using phage  $\Phi 29$  DNA polymerase, which reduces the bacterial and human DNA content in the sample. Illumina sequencing and data analysis identified 478 contigs that were presumed to be DNA viruses. 60 of these contigs could be assembled into circles, indicating that the whole circular genome of some viruses was covered by the analysis. 87% of the contigs showed no overlap with previously identified viruses, and 13% belonged to phage families, including *Microviridae*, *Podoviridae*, *Myoviridae* and *Siphoviridae*. No known human viruses were recovered, indicating that the gut virome of healthy humans consists mostly of phages.

“ viral populations ... undergo rapid evolution, giving rise to new phage species. ”

Notably, 80% of the contigs persisted over the whole study period, indicating a global stability of the virome. However, individual contigs exhibited high evolution rates: contigs from the family *Microviridae*, for example, exhibited more than  $10^{-5}$  substitutions per nucleotide per day. The genome of the main *Microviridae* family variant differed by 4% between the start and the end of the study and thus can be considered to have evolved into a new species. Other phages, which rely on the high-fidelity replication machinery of the bacterial host, showed less variation. In addition, diversity-generating retroelements and CRISPR (clustered regularly interspaced short palindromic repeats) arrays encoded in viral genomes also contributed to variation over time.

So, the healthy human gut virome consists mainly of long-term resident phages that can rapidly evolve, contributing to variation between individuals.

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**ORIGINAL RESEARCH PAPER** Minot, S. et al. Rapid evolution of the human gut virome. *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1300833110> (2013)

**FURTHER READING** Reyes, A. Going viral: next-generation sequencing applied to phage populations in the human gut. *Nature Rev. Microbiol.* **10**, 607–617 (2012)