## Global phylogeography and ancient evolution of the widespread human gut virus crAssphage

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## **Abstract**

Microbiomes are vast communities of microorganisms and viruses that populate all natural ecosystems. Viruses have been considered to be the most variable component of microbiomes, as supported by virome surveys and examples of high genomic mosaicism. However, recent evidence suggests that the human gut virome is remarkably stable compared with that of other environments. Here, we investigate the origin, evolution and epidemiology of crAssphage, a widespread human gut virus. Through a global collaboration, we obtained DNA sequences of crAssphage from more than one-third of the world's countries and showed that the phylogeography of crAssphage is locally clustered within countries, cities and individuals. We also found fully colinear crAssphage-like genomes in both Old-World and New-World primates, suggesting that the association of crAssphage with primates may be millions of years old. Finally, by exploiting a large cohort of more than 1,000 individuals, we tested whether crAssphage is associated with bacterial taxonomic groups of the gut microbiome, diverse human health parameters and a wide range of dietary factors. We identified strong correlations with different clades of bacteria that are related to Bacteroidetes and weak associations with several diet categories, but no significant association with health or disease. We conclude that crAssphage is a benign cosmopolitan virus that may have coevolved with the human lineage and is an integral part of the normal human gut virome...

## Keywords

Bacteriophages, Environmental microbiology, Microbiome.