

# Unveiling the Mysteries of Gut CrAssphages: A Step Forward in Understanding the Human Virobiome

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A recent study published in the journal Nature and as preprint has revealed a new structural atlas of gut crAssphages, a type of virus that is commonly found in the human gut microbiome.<sup>1,2</sup> This ground breaking research sheds light on the structure and function of these viruses, which play a crucial role in the ecology of the human gut microbiome. The human gut microbiome is a complex and diverse ecosystem of microorganisms that play an important role in human health and disease. Viruses, including crAssphages, are an integral part of this ecosystem, but their structure and function have remained poorly understood until now.

The study used a combination of cryo-electron microscopy and bioinformatics analysis to generate a high-resolution structural atlas of gut crAssphages.<sup>1,2</sup> The results revealed a previously unknown structural organization, with unique features that distinguish them from other known viruses. The findings have important implications for understanding the ecology and evolution of the human gut microbiome. The crAssphages play a key role in controlling the populations of gut bacteria,<sup>3,4</sup> and a better understanding of their structure and function could lead to new strategies for manipulating the microbiome to treat or prevent disease. Moreover, this research has significant implications for the field of virology as a whole. The discovery of new viruses and the elucidation of their structures and functions is critical for developing new antiviral therapies and vaccines. However, there are still many unanswered questions about the role of crAssphages in the human gut microbiome.<sup>5-7</sup> For example, it is still unclear how these viruses interact with the host immune system and how they are transmitted from person to person. It is also unclear if crAssphages play any role in influencing the gut-brain and/or gut-cardiac axis. Considering their biphasic role in patients with obesity and metabolic syndrome<sup>8</sup> it is likely that crAssphages may have an influence on gut-brain and/or gut-cardiac axis. Nonetheless, this study represents a significant step forward in understanding the structure and function of

gut crAssphages and their role in the human microbiome. The insights gained from this research could ultimately lead to new strategies for manipulating the microbiome to improve human health and prevent disease.

Gut crAssphages are a type of bacteriophage that were discovered in 2014. They are highly abundant and specifically infect Bacteroidetes bacteria in the human gut. The human gut microbiome is home to a wide variety of bacteriophages, but the characterization of these phages is challenging due to their genetic diversity and the inability to culture many of them. Analysing the metagenomic data from human gut samples previous studies have identified 143 putative CrAss-like phages, that are highly abundant in the human gut. The bioinformatic analysis have revealed that the putative CrAss-like phages exhibited a high degree of genetic diversity, with unique genomic features, such as different integrases and protein domains, suggesting that they may have distinct functions within the gut microbiome, which remains to be investigated.<sup>9</sup> Several new CrAss-like phage subfamilies have also been identified using metagenomic approaches which highlight the potential of this tool for the discovery and characterization of novel gut phages.<sup>5,9-11</sup> It also highlights the relevance of bioinformatic approaches in addressing unmet needs of scientific research which can be validated through experimental work.<sup>4,7,9,10,12,13</sup> Recent studies have suggested that crAssphages may serve as a useful indicator of human faecal pollution in environmental water samples, as they are present in high concentrations in human sewage and are not found in other animals or environmental sources.<sup>3,14</sup> This makes them a potentially valuable tool for monitoring water quality and identifying sources of contamination. Additionally, crAssphages have been found to have an impact on the composition of the gut microbiome, and may play a role in maintaining gut health. Despite their potential importance, relatively little is known about the biology of crAssphages, and more research is needed to fully understand their ecology and impact on human health. The abundance of crAssphages in human gut is evident from studies reporting detection of crAssphages in over 96% of samples and they are measured at significantly higher concentrations than other viral faecal indicators. There is also a strong positive correlation between crAssphages and human viral pathogens such as Human Polyomaviruses (HPyV).<sup>3,4,14</sup> Hence crAssphages are seen as a promising viral faecal indicator for environmental



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health monitoring which can be achieved through development of standardized methods for its detection and interpretation.

This recent study in Nature<sup>1,2</sup> is a major milestone in advancing our understanding of the human microbiome and the role of viruses in this complex ecosystem. The structural atlas of gut crAssphages provides a valuable resource for researchers in the field and paves the way for new discoveries in the future. The potential impact of this research on human health is significant, and it underscores the importance of continued investment in scientific research and innovation.

## CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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