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Editorial

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Gut virome-microbiome interactions across hosts and environments

The Gut microbiome-virome dynamics and interactions Collection highlights gut viruses, mainly bacteriophages, as determinants of microbial community structure and host-relevant functions across human, animal, and environmental systems. The Collection welcomes studies that quantify virus-microbe interactions, evidence-based linking viruses to microbial hosts, characterise infection dynamics, and connect them to ecological or clinical outcomes. It prioritises methodological rigour and translational relevance in diagnostics, surveillance, and phage-based interventions.

Viruses are persistent components of gut ecosystems and can influence microbial community composition, stability, and function through interactions with cellular microbes[1]. Reviews across gastrointestinal conditions describe bacteriophages as important regulators of bacterial populations and as potential modulators of host relevant functions through their effects on bacterial metabolism and immune interactions[2,3]. Alterations in virome composition have been reported in inflammatory bowel disease and are associated with shifts in bacterial communities and clinical features, supporting the need for mechanistic studies that resolve directionality and consequence[4,5]. Evidence from sterile faecal filtrate transplantation trials indicates that phages, acting in conjunction with co-transferred metabolites and other small molecules, can contribute to microbiome state changes that are not captured by bacterial profiling alone[6]. These observations motivate a shift from descriptive catalogues of viral sequences toward studies that quantify virus-microbe interactions, characterise infection strategies, and link viral features to measurable ecological or clinical outcomes.

The Collection promotes research that moves beyond descriptive virome profiles to define interaction processes and their consequences for ecosystem function and host relevant phenotypes (Fig. 1). This editorial introduces the One Health scope, outlines expectations for host linking and infection dynamics, and discusses functional and translational implications.

A One Health view of gut viromes

Gut associated viruses circulate within connected human, animal, and environmental systems. A One Health framing, which recognises the interconnection of human, animal, and environmental health, supports comparative analysis across hosts and environments supports comparative analysis across hosts and environments and strengthens interpretation by incorporating exposure pathways and shared ecological drivers[7,8] Applying these concepts to gut viromes can inform questions on host range, cross species transmission and shared determinants of virome structure. Non-human gut systems offer important opportunities for mechanistic insight. A recent study of prophages in the pig intestinal tract reported extensive prophage diversity and functional gene repertoires that are likely to influence bacterial fitness and adaptation[9].

Environmental matrices, particularly wastewater, extend this framework to population scale surveillance. A global wastewater metagenomics study across 62 cities reported large numbers of gut associated viruses and consistent geographical patterns, supporting wastewater as a practical matrix for monitoring viral circulation and response to interventions[10]. Wastewater also concentrates viral particles at levels exceeding those typically found in the human gut, making it a practical matrix for phage isolation and cultivated phage characterisation alongside sequence-based surveillance[11,12]. Outbreak focused studies further demonstrate the value of wastewater virome analysis for tracking specific enteric viruses during defined public health events[13–15]. Within this Collection, environmental studies are encouraged when they are linked to gut biology and infection ecology, rather than limited to general viral inventories.

Traditional cultivation-dependent phage isolation, while essential for functional characterisation, is inherently constrained by the cultivability of host bacteria and recovers only a fraction of environmental phage diversity. Sequencing-based metagenomics circumvents these biases to access uncultivated viral populations (so-called viral dark matter) and remains the primary route for discovery at the scale required to understand gut virome ecology across host and environmental systems[16,17].

While the Collection's primary focus is the gut virome, comparative insights from other human microbiome niches can illuminate shared mechanisms and ecological principles. Studies of the oral virome have documented structured phage communities with diverse host associations, encoding AMGs and virulence factors with potential roles in shaping oral bacterial ecology and as biomarkers for disease[18–20]. Similarly, respiratory virome studies have characterised phage communities in the airways whose composition shifts under conditions of dysbiosis and chronic disease, offering analogous frameworks for understanding how viral community changes relate to bacterial community state and host phenotype[21]. Submissions drawing on non-gut systems are welcomed where they provide mechanistic insight applicable to gut virome biology.

From presence to interaction: virus-host links, infection dynamics and functional consequences

Interpreting gut virome data requires more than an inventory of viral sequences because ecological interpretation depends on the identity, traits and abundance of the host[22]. Host linking therefore sits at the centre of this Collection.

CRISPR spacer matching provides one widely used approach. Early work showed that CRISPR arrays in human gut bacteria contain spacers that match known and novel phages, indicating prior encounters and potential host associations[23]. Subsequent work has evaluated performance and proposed criteria for higher confidence matches, including limited mismatches, multiple independent spacers and consideration of spacer position within arrays[24,25]. Submissions using CRISPR based host linkage should state criteria explicitly and discuss potential sources of false assignment.

Prophage context offers another line of evidence. Long read metagenomics improves

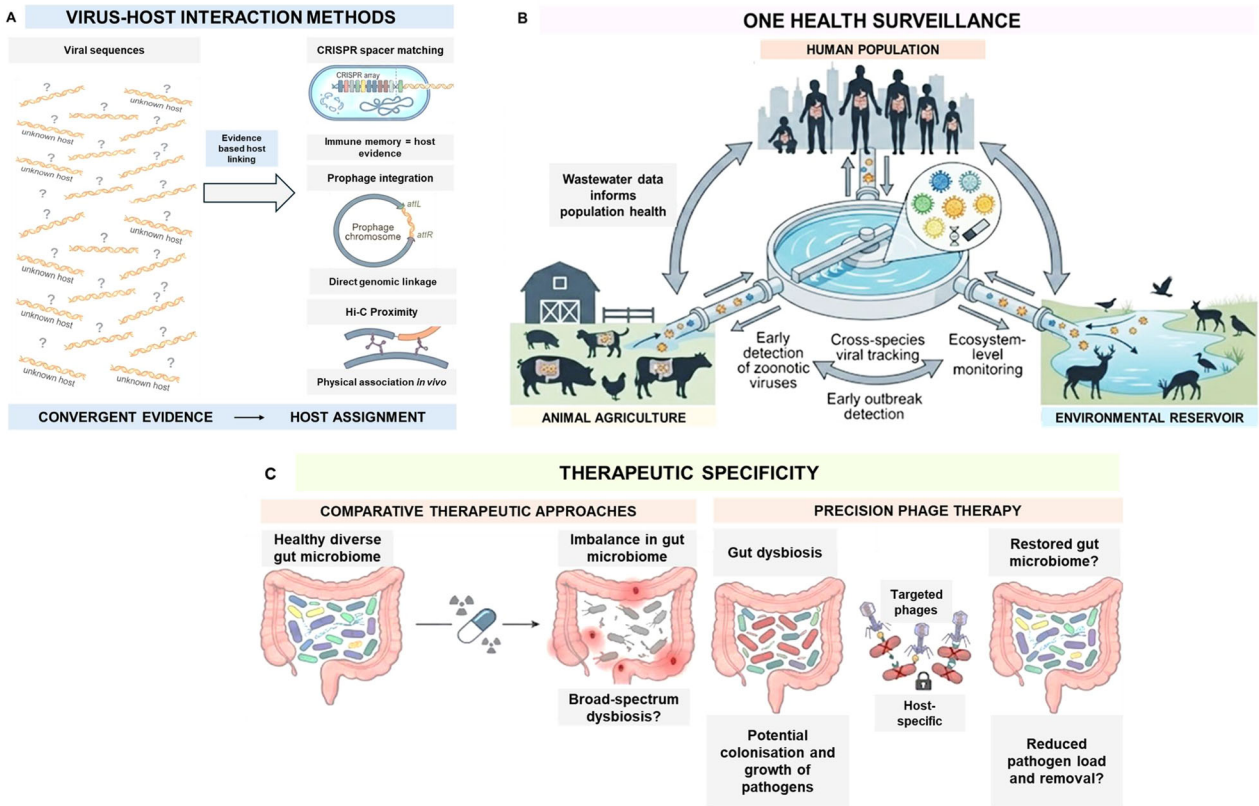

Fig. 1 | Framework for the Gut microbiome-virome dynamics and interactions Collection. A Host linking approaches including CRISPR spacer matching, prophage integration, and Hi C proximity, emphasising convergent evidence for host assignment. **B** One Health surveillance integrating human, animal, and environmental signals through wastewater-based monitoring. **C** Therapeutic specificity contrasting broad spectrum antimicrobials with host specific phage approaches and highlighting infection dynamics relevant to intervention design. Created with BioRender.com.

recovery of complete prophages together with bacterial host chromosomes, enabling direct host assignment and analysis of integration sites and local context[9]. Infant gut virome studies using improved assembly and curation have similarly reported diverse prophage populations and associations with host taxa[26,27]. These approaches are particularly informative for temperate phages that persist in lysogenic states.

Physical proximity-based methods, including metagenomic Hi-C and related techniques, can associate viral and bacterial genomes that are cross linked within the same cellular or spatial context[28,29]. Work in gut environments indicates that these approaches can improve host assignment relative to sequence similarity alone, particularly when combined with CRISPR and prophage evidence[30]. The Collection encourages authors to combine evidence sources where feasible or to provide orthogonal validation where constrained. Claims should report evidence type, thresholds and confidence measures, and state remaining uncertainty.

Understanding host linkage is necessary but not sufficient. Studies should also describe infection processes and consequences for microbial communities and hosts. Temperate phages are relevant to gut ecosystems because they can integrate into bacterial genomes, influence host gene expression and phenotype, and enter lytic cycles in response to environmental conditions[31]. Submissions are encouraged to connect infection dynamics to community level outcomes and, where relevant, host readouts.

Therapeutic specificity and translational work

Therapeutic applications motivate much gut virome research, particularly where conventional antimicrobials are limited by resistance or collateral effects on commensal communities. Reviews focusing on intestinal infections summarise clinical experience with phage therapy and identify practical challenges and evidence gaps[32]. Resource efforts, including curated collections of phages targeting gut associated pathogens and commensals, support rational phage selection and comparison across studies[33]. Translational studies in this Collection should link clinical or phenotypic outcomes to measured changes in virus–host interactions and microbial community structure. Appropriate controls, including antibiotic comparators where relevant, are important for distinguishing specific phage effects from non-specific changes.

The Collection also welcomes work assessing phage-based approaches alongside other microbiome directed strategies, including defined bacterial consortia, prebiotics and dietary interventions, with monitoring of community stability and resistance evolution. Studies proposing virome based diagnostics or biomarkers should report performance characteristics and evaluate robustness across populations and sampling conditions.

Quantitative and experimental work has shown that lytic and temperate strategies can coexist in dynamic bacterial populations, and that infection strategy and induction dynamics

can be measured in situ[34,35]. Functional effects of phage activity and gene carriage are receiving increasing attention. Reviews linking bacteriophages to microbial pathways and cardiometabolic traits propose testable routes connecting phage related functions to host phenotypes[36]. Marine studies have established the relevance of phage encoded auxiliary metabolic genes for redirecting host metabolism and influencing ecosystem processes[28]. Animal gut studies extend this concept by showing that prophages can carry genes related to antibiotic resistance and host interaction that may benefit bacterial hosts under specific conditions[37]. The Collection seeks studies that test expression and impact rather than relying on annotation alone, including designs that manipulate prophage induction, integrate metabolite measurements, or relate infection dynamics to clinical outcomes or treatment responses.

Methodological expectations for submissions

Since inference depends strongly on analytic choices, the Collection sets methodological expectations as guidance. Viral genome quality is a prerequisite for robust ecological inference. Submissions should report genome completeness and contamination estimates, ideally using tools such as CheckV, and should clearly distinguish between complete genomes, high-quality drafts, and fragmented viral contigs[38]. Functional interpretations, including host linkage, lifestyle prediction, and AMG annotation, should be qualified in relation to assembly quality, since fragmented contigs carry greater uncertainty in genomic context. Auxiliary metabolic gene (AMG) annotation requires assignments to be evaluated in genomic context, with attention to proximity to viral hallmark genes and the potential for host chromosomal contamination in assembled contigs. Submissions relying on AMG-based functional inference should report the annotation pipeline, thresholds applied, and any manual curation steps[39].

Host linkage should, where feasible, be supported by more than one evidence type. At minimum, authors should state host assignment criteria, discuss alternative hosts and provide sensitivity analyses. Over interpretation of weak or indirect signals is a common limitation[40,41]. Trans-kingdom bioinformatics pipelines, including Phanta[42] and Marker-MAGu[43], enable simultaneous profiling of phages and bacterial hosts directly from metagenomic sequencing data, supporting the interaction-centred analyses this Collection prioritises. The field is developing rapidly and further tools extending this capacity to multi-omic datasets continue to emerge. Correlation in abundance alone is insufficient where shared determinants can generate co-variation. Abundance estimates should account for compositional effects, sequencing depth variation and sample processing bias. Reporting of negative controls, spike in controls where used, and read mapping and normalisation choices is encouraged. For wastewater and other environmental matrices, authors should report limits of detection, concentration efficiency and inhibition controls[40].

Metadata completeness is essential. Submissions should describe host characteristics, sampling strategy, exposures and storage conditions. Longitudinal studies should specify sampling intervals, handling of missing time points and statistical approaches used to separate temporal trends from noise. Transparent reporting supports synthesis across studies and improves long term value.

The Collection also welcomes computational and mathematical approaches that generate novel biological insight in the absence of new experimental data. Modelling frameworks, including ecological models of phage-bacteria population dynamics, evolutionary simulations of host range shifts, and network-based analyses of virome structure, can reveal emergent properties of phage-microbe systems that are difficult to observe empirically[44–46]. Such approaches are of particular interest when applied across human, animal, and environmental contexts, where phage and bacterial genomes may diverge subtly as they move through different selective environments. Submissions taking this route should describe model assumptions, parameter sources, and sensitivity analyses explicitly.

Conclusion

The Gut microbiome virome dynamics and interactions Collection brings together work that treats gut viruses as integral components of host associated microbial ecosystems. It promotes a One Health view integrating human, animal and environmental domains, including wastewater-based surveillance when linked to gut biology, and it emphasises quantitative evidence for host linkage, infection dynamics and functional consequences. Through this focus, the Collection seeks to strengthen inference and reproducibility and to inform surveillance, diagnostics and phage based or other virome centred interventions.

Data availability

No datasets were generated or analysed during the current study.

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Competing interests
The authors declare no competing interests.