viruses

MDPI

Review

Unraveling the Rectal Virome: Microbial Crosstalk, Immune Modulation, and Clinical Outcomes in People with and Vulnerable to HIV

Ruth S. Bako * and Colleen F. Kelley

The Hope Clinic, Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, 500 Irvin Ct, Suite 200, Decatur, GA 30030, USA; colleen.kelley@emory.edu

* Correspondence: ruth.bako@emory.edu; Tel.: +1-404-422-9386

Abstract

The rectal mucosa houses a large number of viruses with important roles in shaping the local microbial communities and modulating immune responses, which could influence host susceptibility to infection and other diseases. Unique composition of the gut microbiome, including the predominance of clinically significant eukaryotic viruses like herpesviruses, cytomegalovirus, and human papillomavirus, has been described in both people with HIV (PWH) and men who have sex with men (MSM) vulnerable to HIV. Despite these insights, the rectal virome and the clinical implications of virome–bacteriome–immune interactions in the rectal mucosa remain poorly understood. In this review, we synthesize existing data on the composition of the rectal virome, its interactions with the bacteriome and the immune system, and implications on clinical outcomes in people living with or vulnerable to HIV. We also highlight the gaps and research needed to further explore and unravel these relationships.

Keywords: virome; bacteriome; microbiome; immunity; HIV; bacteriophages; eukaryotic viruses

1. Introduction

The gut virome is predominantly composed of bacteriophages, and to a lesser extent, eukaryotic viruses and plant viruses of dietary origin [1–4]. Besides shaping local microbial communities [5] and contributing to disease pathogenesis [6,7], the gut virome has emerging therapeutic potential, including fecal virome transplant and phage therapy [5,8–14]. Furthermore, alterations in the gut viral communities may also serve as novel biomarkers for disease states, given their role in maintaining gut homeostasis [15–18]. The relationship between the virome, bacteriome, and the host immune system has led to the proposed "tri-kingdom network" involving interacting bacteria, phages, and human cells (Figure 1) [19,20]. A disequilibrium in this network, called gut dysbiosis, has been observed across many chronic inflammatory disease states, including inflammatory bowel disease [21–26], cancers [27–29], and neurodegenerative diseases [30–35]. Despite efforts to specifically characterize the gut virome, large parts of the virome remain unclassified, which has been referred to as the "viral dark matter" [2,36,37]. Additionally, questions remain unanswered among the well-characterized parts, such as the degree to which phage-bacteriome-immune interactions are affected in the presence of chronic inflammation induced by HIV and other eukaryotic viruses, and whether phage-induced

Check for updates

Academic Editors: Mimi Ghosh, Raina Nakova Fichorova and Christina Farr

Received: 31 January 2026
Revised: 22 April 2026
Accepted: 25 April 2026
Published: 29 April 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

gut dysbiosis could potentially contribute to the acquisition of sexually transmitted infections (STIs) in those who engage in receptive anal intercourse (RAI). Therefore, significant knowledge gaps persist in our understanding of the gut virome and its overall impact on human health.

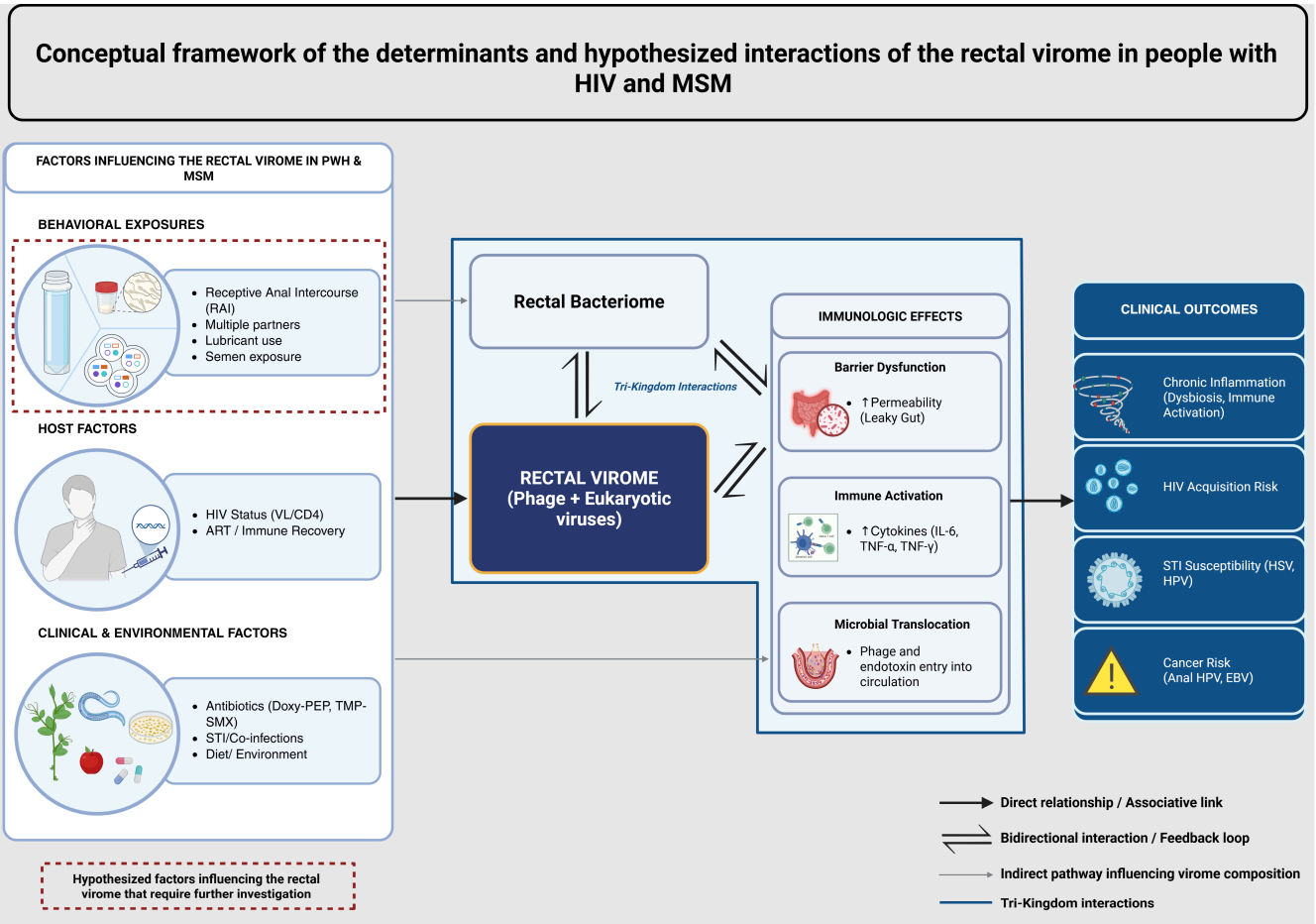


Figure 1. Created in BioRender. A conceptual framework summarizing the determinants and hypothesized interactions of the rectal virome in people with HIV and MSM. The rectal virome in PWH and MSM is predominantly composed of bacteriophages and eukaryotic viruses. The virome is shaped by many factors, including behavioral exposures (e.g., receptive anal intercourse, semen exposure, lubricant use), host factors (e.g., HIV status, immune function, antiretroviral therapy), and clinical/environmental influences (e.g., antibiotic exposure, co-infections, diet). These factors either directly influence the rectal virome or indirectly alter the virome through perturbations in the bacteriome and the host's immune system. Bidirectional interactions among the virome (phages), the bacteriome, and immune cells (Tri-kingdom interactions) can lead to immunologic effects, including epithelial barrier dysfunction, immune activation, and microbial translocation. Consequently, these immunological changes can lead to chronic inflammation (dysbiosis, immune activation), increased HIV acquisition risk, increased STI susceptibility (HSV, HPV), and increased cancer risk (EBV-induced lymphoproliferation, HPV-induced anorectal cancer). The influence of behavioral exposures on the virome has been inferred from related microbiome or sexual exposure studies; limited evidence exists on their direct impact on the rectal virome, which requires further investigation.

Among men who have sex with men (MSM) and particularly among those living with HIV (people with HIV; PWH), prior studies have reported increased prevalence of clinically relevant viruses including herpes simplex virus (HSV), Epstein–Barr virus (EBV), cytomegalovirus (CMV), and human papillomavirus (HPV), as well as anelloviruses and adenoviruses [38–46]. The presence of these viruses in the gut can be linked to clinical out-

comes (e.g., EBV-induced lymphoproliferation, HPV-induced anorectal cancer, and CMV retinitis) [47–49] as well as transmission during condomless RAI. Alterations in the gut bacteriome have also been demonstrated both in PWH as well as MSM vulnerable to HIV who are engaging in RAI, exemplified by a high relative abundance of *Prevotella* [50–52]. Gut dysbiosis is thought to contribute to the chronic inflammation observed in PWH [53]. Building on studies that have demonstrated microbial transfer during sexual contact [54–57], we propose that among MSM both with and without HIV, the rectum may function as part of a potential rectal–penile interface, which represents a microbial and viral transmission nexus where interpersonal virome and bacteriome exchange may occur during RAI. Therefore, the rectum represents both a gut mucosal and a sexual exposure site whose viral populations are not only influenced by diet and digestion, environment, and the resultant local immune responses, as in the rest of the gut virome [2,58–64], but potentially also by sex, semen exposure, lubricants, and partner penile microbiota exposure (Figure 1), making it distinct from other mucosal surfaces in the gut [65–67].

Given the unique characteristics of the bacteriome and virome among MSM with and without HIV, it is important to further explore how the rectal virome influences the bacteriome and mucosal immune changes and its contribution to chronic inflammation and other clinical outcomes in people living with or vulnerable to HIV.

2. Composition, Diversity, and Functional Dynamics of the Gut Virome

The human gut contains the most abundant collection of viruses across the human body, consisting of both DNA and RNA viruses [2,4]. The gut virome is not present at birth; the neonatal gut rapidly acquires its virome after membrane rupture and delivery, marking the first major exposure to the external environment [68–70]. This early period is very critical and may have implications for healthy gut development [58,71]. The initial composition of the infant virome is influenced not only by viruses present in the maternal gut and breast milk, but also by viruses from other maternal body sites, the mode of delivery, the individuals the infant comes into contact with, and the surrounding environment, depicting the role of environmental exposure in shaping the virome [59,71–75]. The early colonizers of the gut include phages of the newborn gut's bacterial communities, and the virome continues to change with age [4], reflecting shifts in the acquisition and relative abundance of host bacterial species over time. Host genetics and immunity, aging, diet, medication use, and geographical location also play a role in shaping the virome, but environmental factors appear to dominate in their influence over the host's genetics [2,58–64].

The adult human gut virome is generally understood to consist of two major parts: the "Persistent Personal Virome" (PPV) and the "Transiently Detected Virome" (TDV) [1]. The PPV forms the core of an individual's viral community and is highly individualized, as each person carries a unique set of phage populations that differ markedly from those of other individuals [1,76–78]. Aside from individual specificity, the gut virome also shows high temporal stability similar to the bacteriome, lasting for more than 2 years in some cases [1,76,77,79,80]. The *Microviridae* and crAss-like phages of the PPV are among the most stable colonizers of the human gut, infecting common gut microbiota such as *Bacteroides*, *Faecalibacterium*, *Eubacterium*, *Prevotella*, and *Parabacteroides* [1]. By contrast, the TDV represents the more variable and short-lived component of the gut virome. Unlike the PPV, the TDV is not strongly individualized, suggesting that it may be acquired from shared environmental exposures, diet, interpersonal contact, or behavioral transmission [1,64,81,82]. The TDV includes a higher proportion of *Siphoviridae* phages along with smaller viral families such as *Inoviridae*, *Genomoviridae*, *Papillomaviridae*, *Anelloviridae*, and *Virgaviridae* [1,81,83]. TDV phages typically infect bacterial hosts that are less common or more transient in the

gut, including *Streptococcus*, *Clostridium*, *Akkermansia*, *Acinetobacter*, *Listeria*, *Escherichia*, and *Bilophila* [1,81].

Phages are the most abundant members of the gut virome, making up more than 90% of the gut virome (the phageome) [84]. While phages do not infect human cells, they alter bacterial pathogens by transferring virulence factors that promote bacterial infectivity and colonization [19,85–87]. Phage-encoded proteins can also disable phagocytes involved in bacterial immune clearance [88]. Phage-driven virulence has been well documented in pathogens such as *Vibrio cholerae* [89–91] and *Escherichia coli* [92], among others [93,94]. Because of the significance of these phage-bacteria interactions, the use of phage therapy for the treatment of diseases, including STIs, is a growing area of research, offering a promising approach for the treatment and development of vaccines against these STIs [95–97]. Researchers have used engineered phages to slow the growth and reduce the infectivity of *Chlamydia trachomatis* [98–100], but similar findings are yet to be discovered for *Neisseria gonorrhoeae* [101,102] and *Treponema pallidum*. This gap highlights an important area for future research. In this era of treatment failure due to antibiotic resistance [103–105], understanding these phage-bacteria interactions is particularly relevant given the increased prevalence of these STIs in the rectal mucosa of MSM [106,107].

Phages also function as active immunomodulators, with direct and indirect effects on human host immunity (Figure 2). They adhere to mucus and form a protective mucosal layer, providing a non-host-derived form of immunity that protects host cells from bacterial-induced damage [108,109]. Alternatively, phages can disrupt the intestinal barrier by altering the bacteriome and increasing intestinal permeability, thereby permitting the translocation of bacterial endotoxins through this compromised barrier [110]. Upon crossing the gut epithelium into the circulation, phages interact with both innate and adaptive immunity by influencing immune signaling, including cytokine release, bacterial recognition, and T- and B-cell regulation [111–115]. Researchers have demonstrated that phage-induced gut dysbiosis and leaky gut contribute to many diseases, such as inflammatory bowel disease [21–26], Alzheimer's disease [30–35], diabetes [116,117], and other diseases characterized by chronic inflammation [110]. This is relevant to PWH, where bacterial translocation is thought to be a major driver of chronic inflammation, and chronic immune activation and mucosal barrier dysfunction are central to disease progression [118–120]. It is possible that the impaired gut mucosal barrier observed in HIV infection favors phage DNA translocation [121], thereby creating an environment that amplifies phage-bacteriome and phage-immune interactions.

Phage-driven horizontal gene transfer can facilitate the movement of antibiotic resistance genes (ARGs), although ARG carriage within human phageomes appears limited [122–124]. Antibiotic exposure has also been shown to perturb the bacteriome, drive rapid shifts in phage communities, and promote the transfer of virulence factors [6,61,122–129]. PWH, particularly those with advanced disease ($CD4^+$ T-cell count < 200 cells/μL), frequently experience recurrent bacterial infections and sexually transmitted infections, and therefore often receive repeated courses of antibiotics or long-term prophylaxis to prevent opportunistic infections [130,131]. Among MSM, higher rates of bacterial STIs similarly contribute to higher antibiotic use [132–134]. In this group, the increasing uptake of post-exposure prophylaxis with doxycycline (Doxy-PEP) for STI prevention represents an additional and ongoing source of antibiotic exposure [135–138]. Despite this, it remains unclear whether chronic antibiotic exposure meaningfully alters the rectal virome in PWH and/or MSM, or whether such changes have downstream effects on mucosal inflammation, local immunity, or systemic immune activation.

We summarize the key mechanistic pathways linking the gut/rectal virome to immune modulation and clinical outcomes in PWH and MSM in Table 1. Table 1 provides an

overview of proposed mechanisms by which the rectal virome interacts with the host's immune system and their potential clinical implications in PWH and MSM.

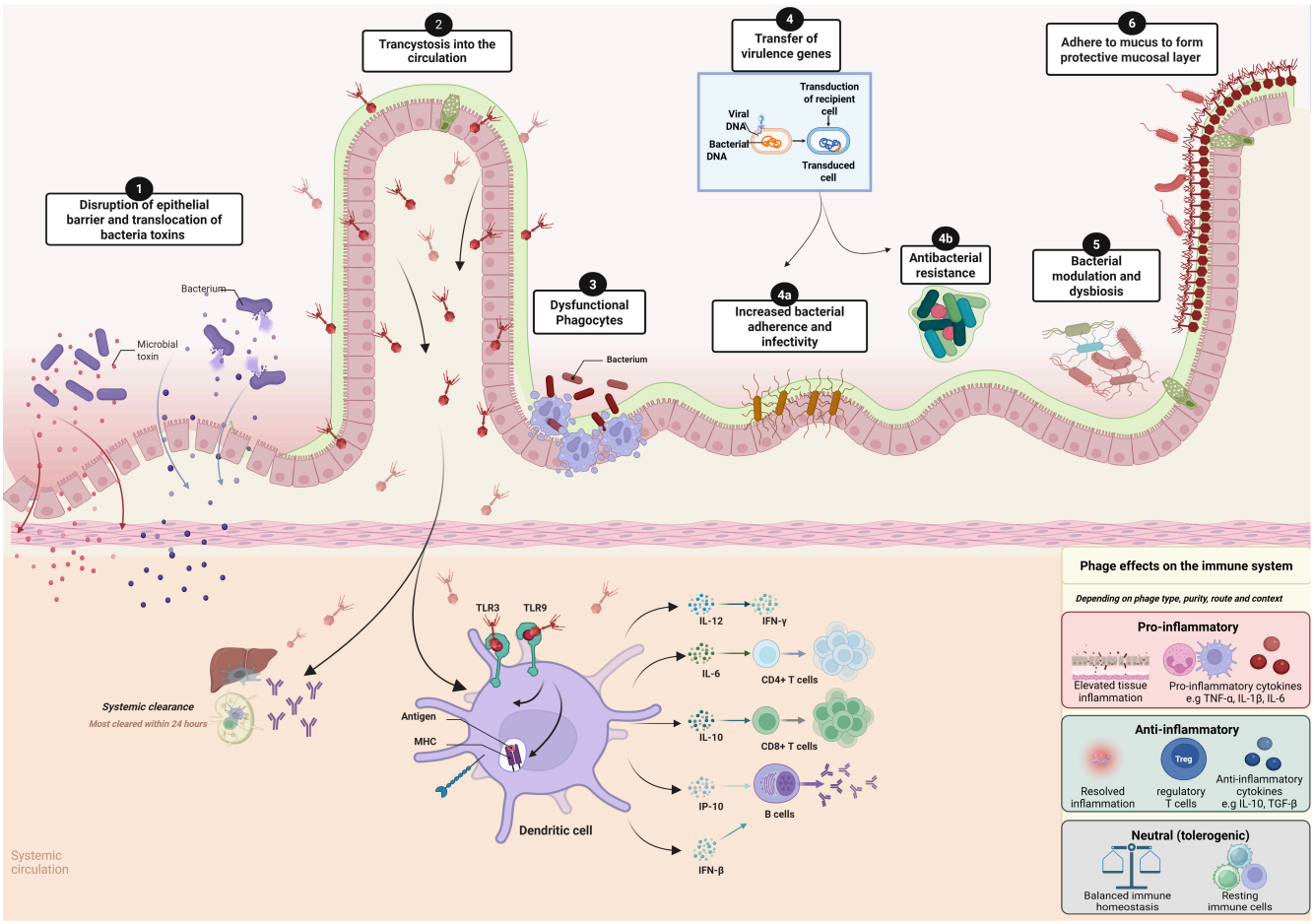


Figure 2. Created in BioRender. Interactions between bacteriophages, the intestinal epithelium, and host immune responses. Bacteriophages interact and influence gut homeostasis and host immunity through multiple pathways, including (1) disruption of epithelial barrier integrity, permitting translocation of bacteria and their toxins; (2) transcytosis across the intestinal epithelium into systemic circulation, and subsequent downstream cytokine signaling and activation of the innate and adaptive immune pathways through recognition by TLRs on antigen-presenting dendritic cells; (3) dysfunction of phagocytes involved in bacterial immune clearance; (4) phage-mediated horizontal gene transfer, which can enhance bacterial virulence and antibiotic resistance (4a,4b); (5) modulation of bacterial communities through lytic or lysogenic conversion resulting in bacterial dysbiosis; and (6) adhere to mucus to form a protective mucosal layer protecting against bacteria invasion.

Table 1. Mechanistic Pathways Linking the Gut/Rectal Virome to Immune Modulation and Clinical Outcomes in People With and Vulnerable to HIV.

Proposed Mechanistic Pathway	Viral/Phage Group Involved	Immunologic/Biologic Effect	Possible Clinical Implications
Protective mucosal layer	Phages [108,109]	Adhere to mucus forming a barrier against bacterial invasion	Reduced bacterial colonization and gut inflammation
Disruption of the epithelial barrier	Phages [110], CMV [39], Adenovirus [40,45], HSV [139]	Breakdown of tight junction and increased gut permeability	Microbial translocation; systemic inflammation and immune activation
Bacterial inhibition and lysis	Phages [98–100]	Lysis of bacterial hosts	Control of pathogenic bacteria; potential therapeutic applications

Table 1. *Cont.*

Proposed Mechanistic Pathway	Viral/Phage Group Involved	Immunologic/Biologic Effect	Possible Clinical Implications
Bacteria competition and selection	Phages [140–142]	Indirect suppression or lysis of competing bacterial species, selective advantage for other bacteria	Dysbiosis; metabolic and inflammatory implications
Immune activation & cytokine dysregulation	Phages [111–115], CMV [39,143], EBV [144–146], HSV [147–149], HPV [150–154]	Chronic immune activation (↑ IL-6, TNF-α, IFN-γ)	Worsening HIV associated inflammation; HIV progression; other comorbidities
Immune suppression/immune evasion	Phages [114], EBV [155–159], GBV-C [160], Anelloviruses [161,162]	Modulation of T-cell function; cytokine mimicry; inhibition of immune clearance	Persistent infection; altered immune recovery
Bacteriome modulation	Phages [6,163,164]	Shifts in bacterial composition; Enhanced metabolic capacities	Dysbiosis; metabolic and inflammatory implications
Horizontal gene transfer & virulence	Phages [6,122–125,164,165]	Transfer of virulence factors, ARGs	Increased bacterial pathogenicity; antimicrobial resistance
Oncogenesis	HPV [48], EBV [146,166,167]	Cellular transformation; chronic inflammation, viral integration into host genome	Anal cancer; lymphoproliferative disease
Enhanced HIV susceptibility	HSV [168–171]	$CD4^+$ T-cell recruitment; mucosal damage	Increased HIV acquisition risk

Future research should explore the contribution of phage-induced immune activation to persistent inflammation seen in HIV infection. Perhaps, establishing this link would deepen our understanding of HIV-associated immune activation and may reveal phage-directed novel therapeutic targets.

3. The Gut Virome in PWH and MSM Vulnerable to HIV Acquisition

3.1. Overview of the Gut Microbiome in PWH and MSM Vulnerable to HIV Acquisition

Prior research has shown that the rectum of MSM who engage in RAI has increased production of pro-inflammatory cytokines and relative abundance of *Prevotella* taxa compared to men who do not engage in RAI [50–52,66,172]. With respect to the virome, the abundance of *Prevotella* in the human gut has been linked to higher viral diversity, greater proportions of temperate phages, and lower total viral genome loads in fecal samples [1], reflecting the close-knit and dynamic relationship between the bacteriome and virome. The bacteriome changes in MSM have been linked to sexual practices including condomless RAI, an increasing number of sexual partners, use of hyperosmolar lubricants, and other behaviors and environmental factors [65–67]. While direct evidence linking these exposures to rectal virome changes remains limited, it is plausible that these exposures and factors are likely to influence the rectal virome, both directly through the introduction of viruses from partner exposures and indirectly through bacteriome shifts, or through other unknown mechanisms, which in turn drive changes in phage populations. These factors are summarized in Table 2 and Figure 1; further studies are needed to characterize these relationships.

Table 2. Plausible Factors that may be Influencing the Rectal/Gut Virome in MSM and People With HIV.

Factors	Virome Impact	Mechanism	Supporting Evidence	Possible Implications
* Receptive anal intercourse (RAI)	Introduction of exogenous viruses/phages	Direct microbial transfer; mucosal exposure; microbiome changes	Microbial transfer studies in sexual partners [54–57] Studies on Microbiome changes in MSM [65,66,173]	Virome diversification; STI risk; Inflammation; Gut dysbiosis
* Semen exposure	Changes in local viral composition	Cytokine signaling; immune modulation	Studies on semen-induced inflammation [174]	Increased immune activation
* Lubricant use (hyperosmolar)	Indirect virome shifts	Epithelial damage, microbiome disruption	MSM microbiome studies [67]	Barrier dysfunction; dysbiosis
Antibiotic exposure (e.g., Doxy-PEP)	Expansion of phage populations	Bacteriome disruption	Antibiotic–phage studies [6,61,122–129,165]	Resistance; dysbiosis
HIV infection	Altered virome diversity	Immune suppression; barrier dysfunction	HIV microbiome/virome studies [175]	Chronic inflammation
ART use	Partial restoration of virome	Immune restoration	Longitudinal HIV studies [40]	Improved immune outcomes
Diet/environment	TDV variability	Environmental viral exposure	Virome ecology studies [2,58–64]	Inter-individual variation

* Mechanisms inferred from related microbiome or sexual exposure studies; there is limited evidence on their direct impact on the rectal virome and require further investigation.

The presence of gut dysbiosis in MSM has also been linked to chronic inflammation and increased acquisition of HIV among MSM [50,51,172,176–179] and perhaps other clinically significant eukaryotic viruses in these groups. During RAI, it is likely that partner-derived bacteria, bacteriophages, and sexually transmitted eukaryotic viruses are transferred into the rectum. The micro-abrasions that occur during RAI [50,51,180,181] may permit deeper entry of viruses, potentiating immune activation [50,51]. While this direct transfer of viruses between the penis and rectum has not been studied, research has demonstrated sharing of genital taxa and bacteriome changes following sexual intercourse among heterosexual couples [54–57,182–185]. Extending this evidence, we hypothesize the concept of a "penile–rectal interface," a bidirectional transmission node where bacterial taxa, phages, and eukaryotic viruses may be exchanged during insertive and receptive anal intercourse. Understanding this interface could reshape our knowledge of the distinct rectal ecosystem that can be observed in MSM and PWH.

Notably, there is limited availability of data relating to the specific gut virome changes that occur in MSM, despite their unique exposures and bacteriome profiles. While some cohorts included MSM participants [40], to date, there are no studies specifically designed to characterize the unique gut virome of MSM, representing a critical gap in the literature.

Studies have also shown that HIV infection has been associated with changes in the gut microbiota [45,186,187], and these changes are significantly different in MSM compared to non-MSM [186]. Chronic HIV infection has been shown to decrease gut levels of *Akkermansia*, *Anaerovibrio*, *Bifidobacterium*, and *Clostridium* [45]. HIV infection also results in the depletion of gut mucosal $CD4^+$ T-cells and Th17 cells [188,189], which are relevant in defense against bacterial invasion and maintaining the intestinal barrier [189,190]. These immune changes have been shown to be amplified by the presence of *Escherichia coli* [191]. Furthermore, HIV is associated with chronic inflammation in the gut primarily due to the loss of $CD4^+$ regulatory T cells (Tregs), which function to maintain homeostasis and modulate the activity of other immune cells [192–194]. The loss of these Tregs has been suggested to contribute to HIV-induced gut dysbiosis. The gut dysbiosis, increased intestinal permeability, and persistent inflammation that occur in HIV infection drive oncogenesis [195] and could permit the translocation of microbial products into the systemic circulation,

further worsening clinical outcomes in these groups. It is unlikely that the effects of HIV are limited to the bacteriome and immune activation, as we do not know the effect of HIV on the phage community in the gut and how these HIV-driven virome changes contribute to chronic inflammation and influence the clinical progression of the disease.

Researchers have demonstrated across various studies that changes in the gut virome occur with HIV infection [45,83,175,196]. Key studies characterizing the gut/rectal virome in people with HIV and MSM are summarized in Table 3. A study reported that severely immunosuppressed people have an increase in adenoviruses in the gut, which might worsen gut mucosal damage [40,45]. Another study found reduced phage diversity in untreated HIV infection that improved after starting antiretroviral therapy (ART) [197]. A recent study also associated dramatic increases in anelloviruses with worsening immune deficiency, returning towards normal levels as the immune system improves [40]. Given that PWH likely have a unique rectal virome, it is possible that shifts within rectal virome composition and diversity could offer a useful surrogate marker for disease progression.

Similarly, because bacterial dysbiosis is linked to advanced HIV infection [45,46], it is plausible that changes in the rectal virome also reflect disease severity, given the close relationship between the bacteriome and the virome. Individuals with advanced HIV disease ($CD4^+$ < 200 cells/μL) have significantly lower gut bacterial diversity (Shannon index) and reduced phage richness (*Inoviridae* bacteriophages) than people with higher $CD4^+$ T-cell counts [40]. *Anelloviridae* [198–200], *Papillomaviridae* [201–204], and *Adenoviridae* [45,175] are also far more abundant in those with advanced HIV. Low $CD4^+$ T-cell counts and the presence of *Anelloviridae* before ART have also been linked to poorer immune recovery [40]. Persistent use of ART (24 months) has also led to a significant drop in the levels of *Anelloviridae* [40]. Therefore, these virome patterns may complement traditional immunologic markers such as blood HIV Viral Load (VL) and $CD4^+$ T-cell counts and provide added insight into immune recovery.

Taken together, gut virome studies in PWH demonstrate that the gut virome alterations in PWH are strongly driven by immune status ($CD4^+$ T-cell depletion), rather than HIV infection alone, and that the virome changes occur alongside reduced bacteriome diversity and enrichment of inflammation-associated taxa, suggesting that HIV-associated gut immune dysfunction drives both virome and bacteriome dysbiosis (Table 3). However, it is worth noting that, despite advances in sequencing techniques, the field is limited by heterogeneity in sequencing techniques. Studies make use of different approaches, including virus-like particle enrichment with short-read sequencing, targeted RT-PCR, and shotgun metagenomics, which vary in their ability to detect certain viral types [205,206]. For instance, the sequencing approach used by Monaco et al. [175] optimized the detection of bacteriophages, but in turn, they lost the ability to detect RNA viruses entirely [196], and while more recent metagenomic methods can permit a broader classification of the virome, they are still limited, as over 90% of the virome remains unannotated [205]. This suggests that improvements in sequencing techniques that allow researchers to detect the full composition of the virome would significantly advance our understanding of the gut virome and its implications on health and diseases among PWH and MSM.

Table 3. Key Studies Characterizing the Gut Microbiome/Virome in People With HIV.

Authors	Population	Sample Site	Sequence Approach	Virome Findings	Bacteriome Findings	Key Drivers	Limitations
Monaco et al., 2016 (Uganda cohort) [175]	82 HIV+, 40 HIV−	Stool	VLP enrichment; NGS; VirusSeeker; 16S rRNA	↑ *Adenoviridae* and *Anelloviridae* in ↓ $CD4^+$ T-cells; virome changes driven by immune status; ↔ bacteriophage communities	↓ richness and diversity in ↓ $CD4^+$ T-cells; ↑ *Enterobacteriaceae*; ↓ *Ruminococcus*	↓ $CD4^+$ T -cell count	Cross-sectional design; no dietary data; unhealthy HIV− controls; RNA virome not assessed; sequencing limitations
Rocafort et al., 2019 (Mozambican Cohort) [45]	147 HIV+, 55 HIV−	Stool	Targeted RT-PCR; 16S rRNA; shotgun metagenomics	↑ adenovirus in early and chronic HIV-1 infection ↔ by ART; ↑ CMV and *Enterovirus* untreated chronic HIV	Transient change in diversity in early HIV, ↓ *Akkermansia*, *Bifidobacterium*, *Clostridium*, and *Anaerovibrio* in chronic HIV; ↓ microbial gene richness in HIV	HIV-related gut immune dysfunction	Limited virome scope; no dietary data
Villoslada-Blanco et al. 2022 (Spanish cohort) [207]	30 HIV+, 26 HIV−	Stool	Shotgun metagenomic sequencing	↓ phage richness partially restored by INSTIs; altered phage β-diversity; ↑ *Caudoviricetes* in untreated HIV; ↑ lysogenic phages	Not assessed	HIV-associated gut inflammation	Cross-sectional design; limited eukaryotic virome power; confounding factors
Boukadida et al., 2024 (Mexico cohort) [40]	92 HIV+ untreated, 53 HIV− controls, longitudinal study of 14 PWH (24 months post-ART)	Stool	16S rRNA sequencing; shotgun metagenomic sequencing	↑ *Anelloviridae*, *Adenoviridae*, *Papillomaviridae* in severe immunodeficiency; ↓ *Tobamovirus*; ↓ *Inoviridae* phages; ART initiation restored virome; Anelloviruses associated with immune recovery	↓ α-diversity; ↑ *Enterococcus*, *Streptococcus*, and *Coprococcus*, in advanced HIV disease; ↑ richness post-ART; ↑ interpersonal variability post-ART	↓ $CD4^+$ T -cell count	No dietary data; confouding factors; small longitudinal sample

Summary of key studies characterizing gut virome and bacteriome alterations in PWH and MS, highlighting methodological approaches used for viral detection, virome findings, key drivers, and limitations. HIV+ = HIV Positive; HIV− = HIV Negative; VLP = Virus-like particle; NGS = Next Generation Sequencing; rRNA = Ribosomal RNA; INSTIs = Integrase Strand Transfer Inhibitors; ↑ = increased; ↓ = decreased; ↔ = unchanged.

3.2. Eukaryotic Viruses of the Gut of PLWH and MSM at Risk of HIV Acquisition

Certain eukaryotic viruses have been detected more commonly in the gut of PWH and MSM. These viruses, reviewed below, may be associated with gut dysbiosis, immune activation, and adverse clinical outcomes (Table 1). Despite significant advances in microbiome research in the gut of PWH and MSM, scientists are only beginning to understand the interactions between these co-morbid eukaryotic viruses (CMV, EBV, HSV, and HPV) and the bacteriome, as well as the rectal mucosal immune system. These discoveries have created a potentially revolutionary niche for advancing our understanding of dysbiotic and inflammatory changes in the gut of PWH and MSM, and for developing targeted, novel therapeutics aimed at improving health outcomes in these groups.

3.2.1. Cytomegalovirus (CMV)

The presence of CMV infection has been associated with a reduction in the ratio of *Firmicutes* to *Bacteroidetes* in the gut during early infection [143]. This ratio is commonly used as a marker of gut dysbiosis, and an abnormal pattern is often seen in people who have inflammatory bowel disease [23,24,208], a pattern that may be observed as relevant in PWH, as both diseases are marked by chronic inflammatory states. CMV co-infection has also been suggested to worsen the progression of HIV infection and to potentiate inflammation even when on suppressive ART [209–212]. CMV can infect the intestinal epithelial cells and disrupt their tight junctions, reducing the barrier integrity and increasing permeability, doing so by triggering the production of pro-inflammatory IL-6 [39]. Several other studies have also demonstrated that CMV triggers inflammatory cytokines like TNF-α, IL-1β, IFN-γ, and IL-6 in several immune and tissue cell types, even in healthy states [143]. This suggests that CMV co-infection may be an important cofactor in driving the gut dysbiosis and chronic inflammation observed in PWHV or MSM.

3.2.2. Epstein–Barr Virus (EBV)

EBV infection has also been associated with gut microbiome shifts and immune activation [144–146]. EBV infection tends to decrease the levels of *Firmicutes* and *Lactobacilli* [144] and to trigger colonic expression of IL-17A, FOXP3, and IFN-γ, all of which are markers of inflammation and autoimmunity [145]. Likewise, the tumorigenic effect of EBV is enhanced by the presence of HIV co-infection [166], and PWH are at increased risk of EBV-induced cancers [167]. EBV's role in causing cancer has also been shown to be due to its ability to infect many immune cells (B cells, T cells, NK cells) and epithelial cells, pushing them to grow uncontrollably [146].

The lifecycle of EBV also involves a latent phase during which its DNA resides in the host cells and consistently triggers cytokine production, producing viral versions of human cytokines (IL-10) to suppress immune activity [146]. While the immune system is unable to completely clear out the infection [213], the immunosuppression that occurs in HIV infection further worsens the clinical outcomes [47,214].

3.2.3. Herpes Simplex Virus (HSV)

The relevance of HSV-associated gut microbiome dysbiosis is particularly important for PWH and MSM, as these groups tend to have a higher prevalence of HSV infection and more frequent episodes of viral reactivation [215–218]. HSV infection has been shown to alter the Firmicutes phylum and certain Clostridium species that produce short-chain fatty acids (SCFAs) [139]. These SCFAs have been found to be essential in maintaining the integrity of the gut barrier and also reducing inflammation [139,219,220]. Treatment with Acyclovir and Intravenous immunoglobulin (IVIG) can further disrupt the bacteriome, leading to significant changes in *Bacteroidetes*, *Firmicutes*, *Akkermansia muciniphila*, *Verrucomi-*

crobia, and other bacterial species [139]. Some of these bacteria have been shown to play a protective role against diseases in human patients [221–225]. HSV-induced gut dysbiosis weakens the blood–brain barrier, activates microglia, and increases inflammation, allowing HSV-1 to reach the brain to establish latent infection and reactivate [149,226].

HSV-1 also infects neurons and releases monocyte chemoattractant protein-1 (MCP-1/CCL2), which attracts macrophages that produce reactive nitrogen species, damaging enteric neurons and causing abnormal gut motility [147,148]. It also induces the expression of viral antigens, which attract activated $CD8^+$ T-cells to the gut [148] and $CD4^+$ T-cells to the genital area [168]. Studies have shown that the mechanism by which HSV increases the acquisition of HIV infection is by recruiting these activated $CD4^+$ T-cells, which are target cells for HIV, and through HSV-induced damage in the mucosal barrier that permits the entry of HIV particles [168–171]. More research is therefore needed to determine how HSV affects the virome and whether the virome-driven changes contribute to the pathogenic effects of HSV infection. There is also a need to identify potential new treatment modalities, given that existing treatments (acyclovir and IVIG) alter the microbiome and may influence long-term clinical outcomes.

3.2.4. Human Papillomavirus (HPV)

The impact of HPV on the gut bacteriome has not been comprehensively explored despite the high burden of anal HPV infection in PWH and MSM [201,227–230]. The majority of the research has focused on the cervicovaginal environment [231–235], where HPV infection results in lower levels of *lactobacilli* and increased levels of bacteria such as *Gardnerella*, *Prevotella*, *Sneathia*, *Megasphaera*, *Streptococcus*, and *Fusobacterium* [233,235]. The resulting cervicovaginal bacteriome dysbiosis weakens the mucosal barrier, increases inflammation, and creates an environment that supports HPV persistence and integration into host DNA [233,236,237]. Studies have shown that women with HPV-induced cervical cancer have higher gut bacteriome α-diversity, differences in the overall composition of gut microbes (β-diversity) [27], and an abundance of *Proteobacteria* [90]. Studies have also shown that the cervical bacteriome and the gut bacteriome may influence how patients respond to cervical cancer treatment and what outcomes they experience [28,238]. Similarly, HPV-related locally advanced SCCA has been associated with higher levels of *Peptoniphilus*, *Fusobacteria*, *Porphyromonas*, and *Prevotella*, suggesting that with anorectal bacteriome changes may be associated with the development of HPV-induced cancer [29].

HPV infects keratinocytes in the epidermis of the skin and the epithelium of the gut and stimulates the production of cytokines (TH1 and TH2) and cytotoxic responses in $CD4^+$ T- and $CD8^+$ T-cells [150–152]. By activating TLRs (TLR9) on keratinocytes, it induces the release of pro-inflammatory cytokines [153,154]. Persistent HPV infection can lead to the transformation of epithelial cells and to the development of warts and cancers [48]. The significant contributions of HPV to morbidity and mortality in PWH and MSM call for prioritized research to better understand the HPV-induced gut bacteriome and virome changes that occur in the gut of these groups and the consequent effects on clinical outcomes. This understanding could guide the development of interventions aimed at reducing the negative impact of HPV on PWH and MSM.

3.2.5. GB Virus C (GBV-C)

GB virus C (GBV-C) is a sexually transmitted lymphotropic eukaryotic virus prevalent among PWH [239–241] and remains a largely unexplored area of virome research in HIV. Although its presence in gut-associated lymphoid tissue (GALT) or fecal samples has not been established, research indicates that it primarily replicates in T and B lymphocytes [242]. The transmission of this virus during RAI needs to be explored, given

that other lymphotropic viruses like HIV can be transmitted through this route [243,244]. Multiple studies have shown that the virus is associated with improved clinical outcomes in PWH [245–249]. GBV-C decreases HIV entry [250,251] and inhibits HIV replication in T cells [252–255]. In addition, it enhances the immune system's response to infection by upregulating interferon expression [256], modulating cytokine signaling [257,258], and regulating $CD4^+$ T-cell apoptosis [259]. However, the mechanism by which this virus modulates the progression of HIV is still poorly understood [260]. Despite these important roles, GBV-C has been rarely considered within the scope of gut or rectal virome research in PWH and MSM. Understanding if sexual behaviors associated with MSM influence GBV-C transmission dynamics, how GBV-C coinfection interacts with local microbial and phage communities, and integrating GBV-C status into virome and bacteriome analyses could inform broader efforts to understand the rectal virome in PWH and MSM.

4. Current Gaps and Future Research Directions

There is no doubt that HIV infection is associated with alterations in the gut virome, yet, how HIV-related immune dysfunction, microbial dysbiosis, and shifts in the virome are linked still remain poorly understood. Despite extensive research on the gut microbiome in MSM vulnerable to HIV and PWH, major gaps remain in our understanding of the rectal virome and how it contributes to mucosal health, immune activation, and clinical outcomes in both groups. This knowledge gap is primarily driven by the lack of a baseline characterization of the rectal virome in PWH and MSM, and the difficulty in establishing causality in the presence of multiple confounding factors like ongoing HIV viral replication, immune deficiency, ART, sexual practices, and antibiotic exposure. There are also very scarce longitudinal data that further complicate our understanding of whether these virome changes are drivers or instead arise as a consequence of chronic inflammation and bacteriome changes. Also, much remains to be learned concerning phage-host relationships within the context of HIV infection and among MSM and their potential as either protective modulators of the mucosal barrier or as contributing factors to inflammation and immune activation. Future studies should include longitudinal designs and integrated multi-omics approaches, including metagenomic and metatranscriptomic sequencing, to comprehensively characterize the gut virome and its interactions with the bacteriome and host immune responses in PWH and MSM.

Author Contributions: Conceptualization, R.S.B. and C.F.K.; writing—original draft preparation, R.S.B.; writing—review and editing, R.S.B. and C.F.K.; visualization, R.S.B.; supervision, C.F.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: No new data were created or analyzed in this study.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

HIV	Human Immunodeficiency Virus
STIs	Sexually Transmitted Infections
RAI	Receptive Anal Intercourse
MSM	Men who have Sex with Men
PWH	People With HIV
HSV	Herpes simplex virus
EBV	Epstein–Barr virus

CMV	Cytomegalovirus
HPV	Human Papillomavirus
DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
PPV	Persistent Personal Virome
TDV	Transiently Detected Virome
crAss	Cross-Assembly
ARG	Antibiotic Resistance Genes
CD4	Cluster of Differentiation 4
Doxy-PEP	Doxycycline Post-Exposure Prophylaxis
Th17	T-helper 17
Tregs	T regulatory cells
ART	Anti-Retroviral Therapy
VL	Viral Load
PWoH	People Without HIV
IL	Interleukin
IFN	Interferon
FOXP3	Forkhead Box P3
NK	Natural Killer
SCFAs	Short-chain fatty acids
CD8	Cluster of Differentiation 8
IVIG	Intravenous Immunoglobulin
MCP	Monocyte Chemoattractant Protein-1
CCL2	C-C Motif Chemokine Ligand 2
SCCA	Squamous cell carcinoma
TH1	T-helper 1
TH2	T-helper 2
TLR	Toll-like receptors
GBV-C	GB Virus C
GALT	Gut-associated lymphoid tissue
VLP	Virus-like particle
NGS	Next Generation Sequencing
rRNA	Ribosmal RNA
INSTIs	Integrase Strand Transfer Inhibitors

References

1. Shkoporov, A.N.; Clooney, A.G.; Sutton, T.D.S.; Ryan, F.J.; Daly, K.M.; Nolan, J.A.; McDonnell, S.A.; Khokhlova, E.V.; Draper, L.A.; Forde, A.; et al. The Human Gut Virome Is Highly Diverse, Stable, and Individual Specific. *Cell Host Microbe* **2019**, *26*, 527–541.e5. [CrossRef]
2. Liang, G.; Bushman, F.D. The Human Virome: Assembly, Composition and Host Interactions. *Nat. Rev. Microbiol.* **2021**, *19*, 514–527. [CrossRef]
3. Zhang, T.; Breitbart, M.; Lee, W.H.; Run, J.-Q.; Wei, C.L.; Soh, S.W.L.; Hibberd, M.L.; Liu, E.T.; Rohwer, F.; Ruan, Y. RNA Viral Community in Human Feces: Prevalence of Plant Pathogenic Viruses. *PLoS Biol.* **2006**, *4*, e3. [CrossRef] [PubMed]
4. Gregory, A.C.; Zablocki, O.; Zayed, A.A.; Howell, A.; Bolduc, B.; Sullivan, M.B. The Gut Virome Database Reveals Age-Dependent Patterns of Virome Diversity in the Human Gut. *Cell Host Microbe* **2020**, *28*, 724–740.e8. [CrossRef] [PubMed]
5. Federici, S.; Nobs, S.P.; Elinav, E. Phages and Their Potential to Modulate the Microbiome and Immunity. *Cell. Mol. Immunol.* **2021**, *18*, 889–904. [CrossRef]
6. Cao, Z.; Sugimura, N.; Burgermeister, E.; Ebert, M.P.; Zuo, T.; Lan, P. The Gut Virome: A New Microbiome Component in Health and Disease. *eBioMedicine* **2022**, *81*, 104113. [CrossRef] [PubMed]
7. Yang, K.; Niu, J.; Zuo, T.; Sun, Y.; Xu, Z.; Tang, W.; Liu, Q.; Zhang, J.; Ng, E.K.W.; Wong, S.K.H.; et al. Alterations in the Gut Virome in Obesity and Type 2 Diabetes Mellitus. *Gastroenterology* **2021**, *161*, 1257–1269.e13. [CrossRef]
8. Ott, S.J.; Waetzig, G.H.; Rehman, A.; Moltzau-Anderson, J.; Bharti, R.; Grasis, J.A.; Cassidy, L.; Tholey, A.; Fickenscher, H.; Seegert, D.; et al. Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients with *Clostridium difficile* Infection. *Gastroenterology* **2017**, *152*, 799–811.e7. [CrossRef]

9. Zuo, T.; Wong, S.H.; Lam, K.; Lui, R.; Cheung, K.; Tang, W.; Ching, J.Y.L.; Chan, P.K.S.; Chan, M.C.W.; Wu, J.C.Y.; et al. Bacteriophage Transfer during Faecal Microbiota Transplantation in Clostridium Difficile Infection Is Associated with Treatment Outcome. *Gut* **2018**, *67*, 634–643. [CrossRef]
10. Duan, Y.; Llorente, C.; Lang, S.; Brandl, K.; Chu, H.; Jiang, L.; White, R.C.; Clarke, T.H.; Nguyen, K.; Torralba, M.; et al. Bacteriophage Targeting of Gut Bacterium Attenuates Alcoholic Liver Disease. *Nature* **2019**, *575*, 505–511. [CrossRef]
11. Kang, D.-W.; Adams, J.B.; Gregory, A.C.; Borody, T.; Chittick, L.; Fasano, A.; Khoruts, A.; Geis, E.; Maldonado, J.; McDonough-Means, S.; et al. Microbiota Transfer Therapy Alters Gut Ecosystem and Improves Gastrointestinal and Autism Symptoms: An Open-Label Study. *Microbiome* **2017**, *5*, 10. [CrossRef]
12. Draper, L.A.; Ryan, F.J.; Smith, M.K.; Jalanka, J.; Mattila, E.; Arkkila, P.A.; Ross, R.P.; Satokari, R.; Hill, C. Long-Term Colonisation with Donor Bacteriophages Following Successful Faecal Microbial Transplantation. *Microbiome* **2018**, *6*, 220. [CrossRef]
13. Broecker, F.; Klumpp, J.; Moelling, K. Long-Term Microbiota and Virome in a Zürich Patient after Fecal Transplantation against Clostridium Difficile Infection. *Ann. N. Y. Acad. Sci.* **2016**, *1372*, 29–41. [CrossRef] [PubMed]
14. Chehoud, C.; Dryga, A.; Hwang, Y.; Nagy-Szakal, D.; Hollister, E.B.; Luna, R.A.; Versalovic, J.; Kellermayer, R.; Bushman, F.D. Transfer of Viral Communities between Human Individuals during Fecal Microbiota Transplantation. *mBio* **2016**, *7*, e00322. [CrossRef] [PubMed]
15. Clooney, A.G.; Sutton, T.D.S.; Shkoporov, A.N.; Holohan, R.K.; Daly, K.M.; O'Regan, O.; Ryan, F.J.; Draper, L.A.; Plevy, S.E.; Ross, R.P.; et al. Whole-Virome Analysis Sheds Light on Viral Dark Matter in Inflammatory Bowel Disease. *Cell Host Microbe* **2019**, *26*, 764–778.e5. [CrossRef]
16. Mangalea, M.R.; Paez-Espino, D.; Kieft, K.; Chatterjee, A.; Chriswell, M.E.; Seifert, J.A.; Feser, M.L.; Demoruelle, M.K.; Sakatos, A.; Anantharaman, K.; et al. Individuals at Risk for Rheumatoid Arthritis Harbor Differential Intestinal Bacteriophage Communities with Distinct Metabolic Potential. *Cell Host Microbe* **2021**, *29*, 726–739.e5. [CrossRef]
17. Kaelin, E.A.; Rodriguez, C.; Hall-Moore, C.; Hoffmann, J.A.; Linneman, L.A.; Ndao, I.M.; Warner, B.B.; Tarr, P.I.; Holtz, L.R.; Lim, E.S. Longitudinal Gut Virome Analysis Identifies Specific Viral Signatures That Precede Necrotizing Enterocolitis Onset in Preterm Infants. *Nat. Microbiol.* **2022**, *7*, 653–662. [CrossRef]
18. Li, Y.; Handley, S.A.; Baldridge, M.T. The Dark Side of the Gut: Virome–Host Interactions in Intestinal Homeostasis and Disease. *J. Exp. Med.* **2021**, *218*, e20201044. [CrossRef] [PubMed]
19. Popescu, M.; Van Belleghem, J.D.; Khosravi, A.; Bollyky, P.L. Bacteriophages and the Immune System. *Annu. Rev. Virol.* **2021**, *8*, 415–435. [CrossRef]
20. Keen, E.C.; Dantas, G. Close Encounters of Three Kinds: Bacteriophages, Commensal Bacteria, and Host Immunity. *Trends Microbiol.* **2018**, *26*, 943–954. [CrossRef]
21. Norman, J.M.; Handley, S.A.; Baldridge, M.T.; Droit, L.; Liu, C.Y.; Keller, B.C.; Kambal, A.; Monaco, C.L.; Zhao, G.; Fleshner, P.; et al. Disease-Specific Alterations in the Enteric Virome in Inflammatory Bowel Disease. *Cell* **2015**, *160*, 447–460. [CrossRef]
22. Fernandes, M.A.; Verstraete, S.G.; Phan, T.G.; Deng, X.; Stekol, E.; LaMere, B.; Lynch, S.V.; Heyman, M.B.; Delwart, E. Enteric Virome and Bacterial Microbiota in Children with Ulcerative Colitis and Crohn's Disease. *J. Pediatr. Gastroenterol. Nutr.* **2019**, *68*, 30–36. [CrossRef] [PubMed]
23. Frank, D.N.; St. Amand, A.L.; Feldman, R.A.; Boedeker, E.C.; Harpaz, N.; Pace, N.R. Molecular-Phylogenetic Characterization of Microbial Community Imbalances in Human Inflammatory Bowel Diseases. *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 13780–13785. [CrossRef]
24. Bálint, A.; Farkas, K.; Méhi, O.; Kintses, B.; Vásárhelyi, B.M.; Ari, E.; Pál, C.; Madácsy, T.; Maléth, J.; Szántó, K.J.; et al. Functional Anatomical Changes in Ulcerative Colitis Patients Determine Their Gut Microbiota Composition and Consequently the Possible Treatment Outcome. *Pharmaceuticals* **2020**, *13*, 346. [CrossRef]
25. Pérez-Brocal, V.; García-López, R.; Vázquez-Castellanos, J.F.; Nos, P.; Beltrán, B.; Latorre, A.; Moya, A. Study of the Viral and Microbial Communities Associated with Crohn's Disease: A Metagenomic Approach. *Clin. Transl. Gastroenterol.* **2013**, *4*, e36. [CrossRef] [PubMed]
26. Zuo, T.; Lu, X.-J.; Zhang, Y.; Cheung, C.P.; Lam, S.; Zhang, F.; Tang, W.; Ching, J.Y.L.; Zhao, R.; Chan, P.K.S.; et al. Gut Mucosal Virome Alterations in Ulcerative Colitis. *Gut* **2019**, *68*, 1169–1179. [CrossRef]
27. Wang, Z.; Wang, Q.; Zhao, J.; Gong, L.; Zhang, Y.; Wang, X.; Yuan, Z. Altered Diversity and Composition of the Gut Microbiome in Patients with Cervical Cancer. *AMB Express* **2019**, *9*, 40. [CrossRef]
28. Sims, T.T.; Colbert, L.E.; Karpinets, T.; Biegert, G.W.G.; Delgado, A.Y.; Mezzari, M.P.; Solley, T.; Yoshida-Court, K.; Mitra, A.; Lin, L.L.; et al. Compositional and Temporal Changes of the Gut Microbiome in Women with Cervical Cancer Undergoing Chemoradiation: Does It Predict Response? *Gynecol. Oncol.* **2020**, *159*, 35–36. [CrossRef]
29. Elnaggar, J.H.; Huynh, V.O.; Lin, D.; Hillman, R.T.; Abana, C.O.; El Alam, M.B.; Tomasic, K.C.; Karpinets, T.V.; Kouzy, R.; Phan, J.L.; et al. HPV-Related Anal Cancer Is Associated with Changes in the Anorectal Microbiome during Cancer Development. *Front. Immunol.* **2023**, *14*, 1051431. [CrossRef]

30. Study Finds Potential Link Between Parkinson's and Gut Health | Parkinson's Foundation. Available online: https://www.parkinson.org/blog/science-news/parkinsons-and-gut-health (accessed on 25 January 2026).
31. Li, Z.; Liang, H.; Hu, Y.; Lu, L.; Zheng, C.; Fan, Y.; Wu, B.; Zou, T.; Luo, X.; Zhang, X.; et al. Gut Bacterial Profiles in Parkinson's Disease: A Systematic Review. *CNS Neurosci. Ther.* **2022**, *29*, 140–157. [CrossRef] [PubMed]
32. Beyond the Brain: The Gut Microbiome and Alzheimer's Disease. Available online: https://www.nia.nih.gov/news/beyond-brain-gut-microbiome-and-alzheimers-disease (accessed on 25 January 2026).
33. Liang, Y.; Liu, C.; Cheng, M.; Geng, L.; Li, J.; Du, W.; Song, M.; Chen, N.; Yeleen, T.A.N.; Song, L.; et al. The Link between Gut Microbiome and Alzheimer's Disease: From the Perspective of New Revised Criteria for Diagnosis and Staging of Alzheimer's Disease. *Alzheimer's Dement.* **2024**, *20*, 5771–5788. [CrossRef]
34. Fonseca, M.d.C.; Zanetti, L.; Fanourakis, S.; Sulzer, D.L.; Mazmanian, S.K. The Gut Microbiome, Systemic Inflammation, and Autoimmunity in Parkinson's Disease. *Lancet Neurol.* **2026**, *25*, 103–114. [CrossRef]
35. Wallen, Z.D.; Demirkan, A.; Twa, G.; Cohen, G.; Dean, M.N.; Standaert, D.G.; Sampson, T.R.; Payami, H. Metagenomics of Parkinson's Disease Implicates the Gut Microbiome in Multiple Disease Mechanisms. *Nat. Commun.* **2022**, *13*, 6958. [CrossRef]
36. Roux, S.; Hallam, S.J.; Woyke, T.; Sullivan, M.B. Viral Dark Matter and Virus–Host Interactions Resolved from Publicly Available Microbial Genomes. *eLife* **2015**, *4*, e08490. [CrossRef] [PubMed]
37. Aggarwala, V.; Liang, G.; Bushman, F.D. Viral Communities of the Human Gut: Metagenomic Analysis of Composition and Dynamics. *Mob. DNA* **2017**, *8*, 12. [CrossRef]
38. Chuerduangphui, J.; Proyrungroj, K.; Pientong, C.; Hinkan, S.; Budkaew, J.; Pimson, C.; Chumworathayi, B.; Hanond, P.; Ekalaksananan, T. Prevalence and Anatomical Sites of Human Papillomavirus, Epstein-Barr Virus and Herpes Simplex Virus Infections in Men Who Have Sex with Men, Khon Kaen, Thailand. *BMC Infect. Dis.* **2018**, *18*, 509. [CrossRef] [PubMed]
39. Maidji, E.; Somsouk, M.; Rivera, J.M.; Hunt, P.W.; Stoddart, C.A. Replication of CMV in the Gut of HIV-Infected Individuals and Epithelial Barrier Dysfunction. *PLoS Pathog.* **2017**, *13*, e1006202. [CrossRef]
40. Boukadida, C.; Peralta-Prado, A.; Chávez-Torres, M.; Romero-Mora, K.; Rincon-Rubio, A.; Ávila-Ríos, S.; Garrido-Rodríguez, D.; Reyes-Terán, G.; Pinto-Cardoso, S. Alterations of the Gut Microbiome in HIV Infection Highlight Human Anelloviruses as Potential Predictors of Immune Recovery. *Microbiome* **2024**, *12*, 204. [CrossRef]
41. van Baarle, D.; Hovenkamp, E.; Dukers, N.H.T.M.; Renwick, N.; Kersten, M.J.; Goudsmit, J.; Coutinho, R.A.; Miedema, F.; van Oers, M.H.J. High Prevalence of Epstein-Barr Virus Type 2 among Homosexual Men Is Caused by Sexual Transmission. *J. Infect. Dis.* **2000**, *181*, 2045–2049. [CrossRef] [PubMed]
42. Lama, J.R.; Lucchetti, A.; Suarez, L.; Laguna-Torres, V.A.; Guanira, J.V.; Pun, M.; Montano, S.M.; Celum, C.L.; Carr, J.K.; Sanchez, J.; et al. Association of Herpes Simplex Virus Type 2 Infection and Syphilis with Human Immunodeficiency Virus Infection among Men Who Have Sex with Men in Peru. *J. Infect. Dis.* **2006**, *194*, 1459–1466. [CrossRef]
43. Goodgame, R.W. Gastrointestinal Cytomegalovirus Disease. *Ann. Intern. Med.* **1993**, *119*, 924–935. [CrossRef] [PubMed]
44. Francis, N.D.; Boylston, A.W.; Roberts, A.H.; Parkin, J.M.; Pinching, A.J. Cytomegalovirus Infection in Gastrointestinal Tracts of Patients Infected with HIV-1 or AIDS. *J. Clin. Pathol.* **1989**, *42*, 1055–1064. [CrossRef]
45. Rocafort, M.; Noguera-Julian, M.; Rivera, J.; Pastor, L.; Guillén, Y.; Langhorst, J.; Parera, M.; Mandomando, I.; Carrillo, J.; Urrea, V.; et al. Evolution of the Gut Microbiome Following Acute HIV-1 Infection. *Microbiome* **2019**, *7*, 73. [CrossRef]
46. Borgognone, A.; Noguera-Julian, M.; Oriol, B.; Noël-Romas, L.; Ruiz-Riol, M.; Guillén, Y.; Parera, M.; Casadellà, M.; Duran, C.; Puertas, M.C.; et al. Gut Microbiome Signatures Linked to HIV-1 Reservoir Size and Viremia Control. *Microbiome* **2022**, *10*, 59. [CrossRef] [PubMed]
47. Bibas, M.; Antinori, A. EBV and HIV-Related Lymphoma. *Mediterr. J. Hematol. Infect. Dis.* **2009**, *1*, e2009032. [CrossRef] [PubMed]
48. zur Hausen, H. Papillomaviruses and Cancer: From Basic Studies to Clinical Application. *Nat. Rev. Cancer* **2002**, *2*, 342–350. [CrossRef] [PubMed]
49. Gallant, J.E.; Moore, R.D.; Richman, D.D.; Keruly, J.; Chaisson, R.E. Incidence and Natural History of Cytomegalovirus Disease in Patients with Advanced Human Immunodeficiency Virus Disease Treated with Zidovudine. The Zidovudine Epidemiology Study Group. *J. Infect. Dis.* **1992**, *166*, 1223–1227. [CrossRef] [PubMed]
50. Kelley, C.F.; Kraft, C.S.; de Man, T.J.B.; Duphare, C.; Lee, H.-W.; Yang, J.; Easley, K.A.; Tharp, G.K.; Mulligan, M.J.; Sullivan, P.S.; et al. The Rectal Mucosa and Condomless Receptive Anal Intercourse in HIV Negative MSM: Implications for HIV Transmission and Prevention. *Mucosal Immunol.* **2017**, *10*, 996–1007. [CrossRef]
51. Van Doren, V.E.; Ackerley, C.G.; Arthur, R.A.; Murray, P.M.; Smith, S.A.; Hu, Y.-J.; Kelley, C.F. Rectal Mucosal Inflammation, Microbiome, and Wound Healing in Men Who Have Sex with Men Who Engage in Receptive Anal Intercourse. *Sci. Rep.* **2024**, *14*, 31598. [CrossRef]
52. Armstrong, A.J.S.; Shaffer, M.; Nusbacher, N.M.; Griesmer, C.; Fiorillo, S.; Schneider, J.M.; Preston Neff, C.; Li, S.X.; Fontenot, A.P.; Campbell, T.; et al. An Exploration of Prevotella-Rich Microbiomes in HIV and Men Who Have Sex with Men. *Microbiome* **2018**, *6*, 198. [CrossRef]

53. Ishizaka, A.; Koga, M.; Mizutani, T.; Parbie, P.K.; Prawisuda, D.; Yusa, N.; Sedohara, A.; Kikuchi, T.; Ikeuchi, K.; Adachi, E.; et al. Unique Gut Microbiome in HIV Patients on Antiretroviral Therapy (ART) Suggests Association with Chronic Inflammation. *Microbiol. Spectr.* **2021**, *9*, e0070821. [CrossRef]
54. Carda-Diéguez, M.; Cárdenas, N.; Aparicio, M.; Beltrán, D.; Rodríguez, J.M.; Mira, A. Variations in Vaginal, Penile, and Oral Microbiota After Sexual Intercourse: A Case Report. *Front. Med.* **2019**, *6*, 178. [CrossRef]
55. Dixon, R.; Egan, S.; Hughes, S.; Chapman, B. The Sexome—A Proof of Concept Study into Microbial Transfer between Heterosexual Couples after Sexual Intercourse. *Forensic Sci. Int.* **2023**, *348*, 111711. [CrossRef]
56. Ghemrawi, M.; Ramírez Torres, A.; Netherland, M.; Wang, Y.; Hasan, N.A.; El-Fahmawi, B.; Duncan, G.; McCord, B. Forensic Insights from Shotgun Metagenomics: Tracing Microbial Exchange during Sexual Intercourse. *Forensic Sci. Int. Genet.* **2025**, *78*, 103266. [CrossRef]
57. Park, D.E.; Mohammadi, A.; Nelson, S.G.; Salazar, J.E.; Bagherichimeh, S.; Aziz, M.; Onos, A.; Villani, J.; Fazel, A.; Tevlin, E.; et al. Post-Coital Dynamics of the Penile and Cervico-Vaginal Genital Microbiome. *Microbiome* **2026**, *14*, 126. [CrossRef] [PubMed]
58. Avellaneda-Franco, L.; Dahlman, S.; Barr, J.J. The Gut Virome and the Relevance of Temperate Phages in Human Health. *Front. Cell. Infect. Microbiol.* **2023**, *13*, 1241058. [CrossRef] [PubMed]
59. Maqsood, R.; Rodgers, R.; Rodriguez, C.; Handley, S.A.; Ndao, I.M.; Tarr, P.I.; Warner, B.B.; Lim, E.S.; Holtz, L.R. Discordant Transmission of Bacteria and Viruses from Mothers to Babies at Birth. *Microbiome* **2019**, *7*, 156. [CrossRef]
60. Reyes, A.; Blanton, L.V.; Cao, S.; Zhao, G.; Manary, M.; Trehan, I.; Smith, M.I.; Wang, D.; Virgin, H.W.; Rohwer, F.; et al. Gut DNA Viromes of Malawian Twins Discordant for Severe Acute Malnutrition. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 11941–11946. [CrossRef] [PubMed]
61. Boling, L.; Cuevas, D.A.; Grasis, J.A.; Kang, H.S.; Knowles, B.; Levi, K.; Maughan, H.; McNair, K.; Rojas, M.I.; Sanchez, S.E.; et al. Dietary Prophage Inducers and Antimicrobials: Toward Landscaping the Human Gut Microbiome. *Gut Microbes* **2020**, *11*, 721–734. [CrossRef]
62. David, L.A.; Maurice, C.F.; Carmody, R.N.; Gootenberg, D.B.; Button, J.E.; Wolfe, B.E.; Ling, A.V.; Devlin, A.S.; Varma, Y.; Fischbach, M.A.; et al. Diet Rapidly and Reproducibly Alters the Human Gut Microbiome. *Nature* **2014**, *505*, 559–563. [CrossRef]
63. Turnbaugh, P.J.; Ridaura, V.K.; Faith, J.J.; Rey, F.E.; Knight, R.; Gordon, J.I. The Effect of Diet on the Human Gut Microbiome: A Metagenomic Analysis in Humanized Gnotobiotic Mice. *Sci. Transl. Med.* **2009**, *1*, 6ra14. [CrossRef] [PubMed]
64. Tobin, C.A.; Hill, C.; Shkoporov, A.N. Factors Affecting Variation of the Human Gut Phageome. *Annu. Rev. Microbiol.* **2023**, *77*, 363–379. [CrossRef] [PubMed]
65. Li, K.; Zeng, H.; Liu, T.; Huo, S.; Zhang, C.; Li, W.; Deng, J.; Zhong, X.; Tao, Y.; Lin, B.; et al. Gut Microbiome as a Potential Mediator Linking Sexual Behaviors to Immune Profiles in HIV-Negative Men Who Have Sex with Men: A Multi-Omics Study. *Front. Immunol.* **2025**, *16*, 1659556. [CrossRef] [PubMed]
66. Huang, K.D.; Amend, L.; Gálvez, E.J.C.; Lesker, T.-R.; de Oliveira, R.; Bielecka, A.; Blanco-Míguez, A.; Valles-Colomer, M.; Ruf, I.; Pasolli, E.; et al. Establishment of a Non-Westernized Gut Microbiota in Men Who Have Sex with Men Is Associated with Sexual Practices. *Cell Rep. Med.* **2024**, *5*, 101426. [CrossRef]
67. Haaland, R.E.; Fountain, J.; Hu, Y.; Holder, A.; Dinh, C.; Hall, L.; Pescatore, N.A.; Heeke, S.; Hart, C.E.; Xu, J.; et al. Repeated Rectal Application of a Hyperosmolar Lubricant Is Associated with Microbiota Shifts but Does Not Affect PrEP Drug Concentrations: Results from a Randomized Trial in Men Who Have Sex with Men. *J. Int. AIDS Soc.* **2018**, *21*, e25199. [CrossRef]
68. Breitbart, M.; Haynes, M.; Kelley, S.; Angly, F.; Edwards, R.A.; Felts, B.; Mahaffy, J.M.; Mueller, J.; Nulton, J.; Rayhawk, S.; et al. Viral Diversity and Dynamics in an Infant Gut. *Res. Microbiol.* **2008**, *159*, 367–373. [CrossRef]
69. Lim, E.S.; Rodriguez, C.; Holtz, L.R. Amniotic Fluid from Healthy Term Pregnancies Does Not Harbor a Detectable Microbial Community. *Microbiome* **2018**, *6*, 87. [CrossRef]
70. Lim, E.S.; Zhou, Y.; Zhao, G.; Bauer, I.K.; Droit, L.; Ndao, I.M.; Warner, B.B.; Tarr, P.I.; Wang, D.; Holtz, L.R. Early Life Dynamics of the Human Gut Virome and Bacterial Microbiome in Infants. *Nat. Med.* **2015**, *21*, 1228–1234. [CrossRef]
71. Kennedy, E.A.; Holtz, L.R. Gut Virome in Early Life: Origins and Implications. *Curr. Opin. Virol.* **2022**, *55*, 101233. [CrossRef]
72. Milani, C.; Casey, E.; Lugli, G.A.; Moore, R.; Kaczorowska, J.; Feehily, C.; Mangifesta, M.; Mancabelli, L.; Duranti, S.; Turroni, F.; et al. Tracing Mother-Infant Transmission of Bacteriophages by Means of a Novel Analytical Tool for Shotgun Metagenomic Datasets: METAnnotatorX. *Microbiome* **2018**, *6*, 145. [CrossRef]
73. Siranosian, B.A.; Tamburini, F.B.; Sherlock, G.; Bhatt, A.S. Acquisition, Transmission and Strain Diversity of Human Gut-Colonizing crAss-like Phages. *Nat. Commun.* **2020**, *11*, 280. [CrossRef] [PubMed]
74. Pannaraj, P.S.; Ly, M.; Cerini, C.; Saavedra, M.; Aldrovandi, G.M.; Saboory, A.A.; Johnson, K.M.; Pride, D.T. Shared and Distinct Features of Human Milk and Infant Stool Viromes. *Front. Microbiol.* **2018**, *9*, 1162. [CrossRef]
75. McCann, A.; Ryan, F.J.; Stockdale, S.R.; Dalmasso, M.; Blake, T.; Ryan, C.A.; Stanton, C.; Mills, S.; Ross, P.R.; Hill, C. Viromes of One Year Old Infants Reveal the Impact of Birth Mode on Microbiome Diversity. *PeerJ* **2018**, *6*, e4694. [CrossRef]
76. Minot, S.; Bryson, A.; Chehoud, C.; Wu, G.D.; Lewis, J.D.; Bushman, F.D. Rapid Evolution of the Human Gut Virome. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 12450–12455. [CrossRef]

77. Reyes, A.; Haynes, M.; Hanson, N.; Angly, F.E.; Heath, A.C.; Rohwer, F.; Gordon, J.I. Viruses in the Fecal Microbiota of Monozygotic Twins and Their Mothers. *Nature* **2010**, *466*, 334–338. [CrossRef]
78. Manrique, P.; Bolduc, B.; Walk, S.T.; van der Oost, J.; de Vos, W.M.; Young, M.J. Healthy Human Gut Phageome. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 10400–10405. [CrossRef]
79. Minot, S.; Sinha, R.; Chen, J.; Li, H.; Keilbaugh, S.A.; Wu, G.D.; Lewis, J.D.; Bushman, F.D. The Human Gut Virome: Inter-Individual Variation and Dynamic Response to Diet. *Genome Res.* **2011**, *21*, 1616–1625. [CrossRef]
80. Broecker, F.; Russo, G.; Klumpp, J.; Moelling, K. Stable Core Virome despite Variable Microbiome after Fecal Transfer. *Gut Microbes* **2016**, *8*, 214–220. [CrossRef] [PubMed]
81. Guerin, E.; Hill, C. Shining Light on Human Gut Bacteriophages. *Front. Cell. Infect. Microbiol.* **2020**, *10*, 481. [CrossRef]
82. Bao, H.; Zhang, H.; Zhou, Y.; Zhu, S.; Pang, M.; Shahin, K.; Olaniran, A.; Schmidt, S.; Wang, R. Transient Carriage and Low-Level Colonization of Orally Administrated Lytic and Temperate Phages in the Gut of Mice. *Food Prod. Process Nutr.* **2020**, *2*, 14. [CrossRef]
83. Cesanelli, F.; Scarvaglieri, I.; De Francesco, M.A.; Alberti, M.; Salvi, M.; Tiecco, G.; Castelli, F.; Quiros-Roldan, E. The Human Virome in Health and Its Remodeling During HIV Infection and Antiretroviral Therapy: A Narrative Review. *Microorganisms* **2025**, *14*, 50. [CrossRef] [PubMed]
84. Shkoporov, A.N.; Hill, C. Bacteriophages of the Human Gut: The "Known Unknown" of the Microbiome. *Cell Host Microbe* **2019**, *25*, 195–209. [CrossRef]
85. Barr, J.J. A Bacteriophages Journey through the Human Body. *Immunol. Rev.* **2017**, *279*, 106–122. [CrossRef]
86. Reyes, A.; Semenkovich, N.P.; Whiteson, K.; Rohwer, F.; Gordon, J.I. Going Viral: Next Generation Sequencing Applied to Human Gut Phage Populations. *Nat. Rev. Microbiol.* **2012**, *10*, 607–617. [CrossRef]
87. Mai-Prochnow, A.; Hui, J.G.K.; Kjelleberg, S.; Rakonjac, J.; McDougald, D.; Rice, S.A. 'Big Things in Small Packages: The Genetics of Filamentous Phage and Effects on Fitness of Their Host'. *FEMS Microbiol. Rev.* **2015**, *39*, 465–487. [CrossRef]
88. Veldkamp, K.E.; Heezius, H.C.J.M.; Verhoef, J.; van Strijp, J.A.G.; van Kessel, K.P.M. Modulation of Neutrophil Chemokine Receptors by Staphylococcus Aureus Supernate. *Infect. Immun.* **2000**, *68*, 5908–5913. [CrossRef]
89. Faruque, S.M.; Mekalanos, J.J. Pathogenicity Islands and Phages in *Vibrio cholerae* Evolution. *Trends Microbiol.* **2003**, *11*, 505–510. [CrossRef] [PubMed]
90. Faruque, S.M.; Mekalanos, J.J. Phage-Bacterial Interactions in the Evolution of Toxigenic Vibrio Cholerae. *Virulence* **2012**, *3*, 556–565. [CrossRef] [PubMed]
91. McLeod, S.M.; Kimsey, H.H.; Davis, B.M.; Waldor, M.K. CTXφ and Vibrio Cholerae: Exploring a Newly Recognized Type of Phage–Host Cell Relationship. *Mol. Microbiol.* **2005**, *57*, 347–356. [CrossRef] [PubMed]
92. Veses-Garcia, M.; Liu, X.; Rigden, D.J.; Kenny, J.G.; McCarthy, A.J.; Allison, H.E. Transcriptomic Analysis of Shiga-Toxigenic Bacteriophage Carriage Reveals a Profound Regulatory Effect on Acid Resistance in *Escherichia coli*. *Appl. Environ. Microbiol.* **2015**, *81*, 8118–8125. [CrossRef]
93. Derbise, A.; Chenal-Francisque, V.; Pouillot, F.; Fayolle, C.; Prévost, M.-C.; Médigue, C.; Hinnebusch, B.J.; Carniel, E. A Horizontally Acquired Filamentous Phage Contributes to the Pathogenicity of the Plague Bacillus. *Mol. Microbiol.* **2007**, *63*, 1145–1157. [CrossRef] [PubMed]
94. Bille, E.; Zahar, J.-R.; Perrin, A.; Morelle, S.; Kriz, P.; Jolley, K.A.; Maiden, M.C.J.; Dervin, C.; Nassif, X.; Tinsley, C.R. A Chromosomally Integrated Bacteriophage in Invasive Meningococci. *J. Exp. Med.* **2005**, *201*, 1905–1913. [CrossRef]
95. Cater, K.; Międzybrodzki, R.; Morozova, V.; Letkiewicz, S.; Łusiak-Szelachowska, M.; Rękas, J.; Weber-Dąbrowska, B.; Górski, A. Potential for Phages in the Treatment of Bacterial Sexually Transmitted Infections. *Antibiotics* **2021**, *10*, 1030. [CrossRef]
96. Durr, H.A.; D. Leipzig, N. Advancements in Bacteriophage Therapies and Delivery for Bacterial Infection. *Mater. Adv.* **2023**, *4*, 1249–1257. [CrossRef]
97. Piekarowicz, A.; Kłyż, A.; Stein, D. A New Vaccination Method Based on Phage NgoΦ6 and Its Phagemid Derivatives. *Front. Microbiol.* **2022**, *13*, 793205. [CrossRef]
98. You, C.; Wang, M.; Wang, J.; Lian, T.; Liu, Q. M13 Phages Engineered with Chlamydia Phage φCPG1 Protein IN5 and Arginine-Glycine-Aspartic Acid Inhibits Chlamydia Trachomatis Intracellular Growth. *Virus Res.* **2025**, *361*, 199645. [CrossRef]
99. Bhattarai, S.R.; Yoo, S.Y.; Lee, S.-W.; Dean, D. Engineered Phage-Based Therapeutic Materials Inhibit Chlamydia Trachomatis Intracellular Infection. *Biomaterials* **2012**, *33*, 5166–5174. [CrossRef]
100. Wei, S.; Liu, Q.; Lian, T.; Shao, L. The ΦCPG1 Chlamydiaphage Can Infect *Chlamydia trachomatis* and Significantly Reduce Its Infectivity. *Virus Res.* **2019**, *267*, 1–8. [CrossRef] [PubMed]
101. Laumen, J.G.E.; Abdellati, S.; Manoharan-Basil, S.S.; Van Dijck, C.; Van den Bossche, D.; De Baetselier, I.; de Block, T.; Malhotra-Kumar, S.; Soentjes, P.; Pirnay, J.-P.; et al. Screening of Anorectal and Oropharyngeal Samples Fails to Detect Bacteriophages Infecting Neisseria Gonorrhoeae. *Antibiotics* **2022**, *11*, 268. [CrossRef] [PubMed]
102. Adamczyk-Popławska, M.; Golec, P.; Piekarowicz, A.; Kwiatek, A. The Potential for Bacteriophages and Prophage Elements in Fighting and Preventing the Gonorrhea. *Crit. Rev. Microbiol.* **2024**, *50*, 769–784. [CrossRef]

103. Broom, A.; Peterie, M.; Ridge, D.; Lafferty, L.; Kenny, K.; Broom, J.; Kelly-Hanku, A.; Treloar, C.; Applegate, T. Sex, Drugs and Superbugs: The Rise of Drug Resistant STIs. *SSM—Qual. Res. Health* **2023**, *4*, 100310. [CrossRef]
104. Giacani, L.; Bradshaw, C.S.; Muzny, C.A.; Graves, K.J.; Pasricha, S.; Jordan, S.J.; Allan-Blitz, L.-T. Antimicrobial Resistance in Curable Sexually Transmitted Infections. *Curr. HIV/AIDS Rep.* **2025**, *22*, 14. [CrossRef]
105. Jensen, J.S.; Unemo, M. Antimicrobial Treatment and Resistance in Sexually Transmitted Bacterial Infections. *Nat. Rev. Microbiol.* **2024**, *22*, 435–450. [CrossRef] [PubMed]
106. Turner, A.N.; Reese, P.C.; Ervin, M.; Davis, J.A.; Fields, K.S.; Bazan, J.A. HIV, Rectal Chlamydia and Rectal Gonorrhea in Men Who Have Sex with Men Attending an STD Clinic in a Midwestern US City. *Sex. Transm. Dis.* **2013**, *40*, 433–438. [CrossRef]
107. Khosropour, C.M.; Coomes, D.M.; LeClair, A.; Saechao, F.; Vorn, S.; Soge, O.O.; Barbee, L.A. High Prevalence of Rectal Chlamydia and Gonorrhea Among Men Who Have Sex with Men Who Do Not Engage in Receptive Anal Sex. *Sex. Transm. Dis.* **2023**, *50*, 404–409. [CrossRef]
108. Barr, J.J.; Auro, R.; Furlan, M.; Whiteson, K.L.; Erb, M.L.; Pogliano, J.; Stotland, A.; Wolkowicz, R.; Cutting, A.S.; Doran, K.S.; et al. Bacteriophage Adhering to Mucus Provide a Non–Host-Derived Immunity. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 10771–10776. [CrossRef]
109. Barr, J.J.; Youle, M.; Rohwer, F. Innate and Acquired Bacteriophage-Mediated Immunity. *Bacteriophage* **2013**, *3*, e25857. [CrossRef]
110. Tetz, G.; Tetz, V. Bacteriophage Infections of Microbiota Can Lead to Leaky Gut in an Experimental Rodent Model. *Gut Pathog.* **2016**, *8*, 33. [CrossRef]
111. Van Belleghem, J.D.; Clement, F.; Merabishvili, M.; Lavigne, R.; Vaneechoutte, M. Pro- and Anti-Inflammatory Responses of Peripheral Blood Mononuclear Cells Induced by Staphylococcus Aureus and Pseudomonas Aeruginosa Phages. *Sci. Rep.* **2017**, *7*, 8004. [CrossRef]
112. Secor, P.R.; Michaels, L.A.; Smigiel, K.S.; Rohani, M.G.; Jennings, L.K.; Hisert, K.B.; Arrigoni, A.; Braun, K.R.; Birkland, T.P.; Lai, Y.; et al. Filamentous Bacteriophage Produced by Pseudomonas Aeruginosa Alters the Inflammatory Response and Promotes Noninvasive Infection In Vivo. *Infect. Immun.* **2016**, *85*, e00648-16. [CrossRef]
113. Hong, Y.; Thimmapuram, J.; Zhang, J.; Collings, C.K.; Bhide, K.; Schmidt, K.; Ebner, P.D. The Impact of Orally Administered Phages on Host Immune Response and Surrounding Microbial Communities. *Bacteriophage* **2016**, *6*, e1211066. [CrossRef]
114. Cafora, M.; Brix, A.; Forti, F.; Loberto, N.; Aureli, M.; Briani, F.; Pistocchi, A. Phages as Immunomodulators and Their Promising Use as Anti-Inflammatory Agents in a *Cftr* Loss-of-Function Zebrafish Model. *J. Cyst. Fibros.* **2021**, *20*, 1046–1052. [CrossRef] [PubMed]
115. Górski, A.; Kniotek, M.; Perkowska-Ptasińska, A.; Mróz, A.; Przerwa, A.; Gorczyca, W.; Dąbrowska, K.; Weber-Dąbrowska, B.; Nowaczyk, M. Bacteriophages and Transplantation Tolerance. *Transplant. Proc.* **2006**, *38*, 331–333. [CrossRef] [PubMed]
116. Ma, Y.; You, X.; Mai, G.; Tokuyasu, T.; Liu, C. A Human Gut Phage Catalog Correlates the Gut Phageome with Type 2 Diabetes. *Microbiome* **2018**, *6*, 24. [CrossRef]
117. Qin, J.; Li, Y.; Cai, Z.; Li, S.; Zhu, J.; Zhang, F.; Liang, S.; Zhang, W.; Guan, Y.; Shen, D.; et al. A Metagenome-Wide Association Study of Gut Microbiota in Type 2 Diabetes. *Nature* **2012**, *490*, 55–60. [CrossRef] [PubMed]
118. Xu, H.; Wang, X.; Veazey, R.S. Mucosal Immunology of HIV Infection. *Immunol. Rev.* **2013**, *254*, 10–33. [CrossRef]
119. Mudd, J.C.; Brenchley, J.M. Gut Mucosal Barrier Dysfunction, Microbial Dysbiosis, and Their Role in HIV-1 Disease Progression. *J. Infect. Dis.* **2016**, *214*, S58–S66. [CrossRef]
120. Brenchley, J.M.; Douek, D.C. The Mucosal Barrier and Immune Activation in HIV Pathogenesis. *Curr. Opin. HIV AIDS* **2008**, *3*, 356–361. [CrossRef]
121. Márquez, M.; Fernández Gutiérrez del Álamo, C.; Girón-González, J.A. Gut Epithelial Barrier Dysfunction in Human Immunodeficiency Virus-Hepatitis C Virus Coinfected Patients: Influence on Innate and Acquired Immunity. *World J. Gastroenterol.* **2016**, *22*, 1433–1448. [CrossRef]
122. Goh, S.; Hussain, H.; Chang, B.J.; Emmett, W.; Riley, T.V.; Mullany, P. Phage ϕC2 Mediates Transduction of Tn6215, Encoding Erythromycin Resistance, between Clostridium Difficile Strains. *mBio* **2013**, *4*, e00840-13. [CrossRef]
123. Mazaheri Nezhad Fard, R.; Barton, M.D.; Heuzenroeder, M.W. Bacteriophage-mediated Transduction of Antibiotic Resistance in Enterococci. *Lett. Appl. Microbiol.* **2011**, *52*, 559–564. [CrossRef]
124. Zhang, Y.; LeJeune, J.T. Transduction of bla_{CMY-2}, Tet(A), and Tet(B) from *Salmonella enterica* Subspecies *enterica* Serovar Heidelberg to S. Typhimurium. *Vet. Microbiol.* **2008**, *129*, 418–425. [CrossRef]
125. Maiques, E.; Úbeda, C.; Campoy, S.; Salvador, N.; Lasa, Í.; Novick, R.P.; Barbé, J.; Penadés, J.R. β-Lactam Antibiotics Induce the SOS Response and Horizontal Transfer of Virulence Factors in Staphylococcus Aureus. *J. Bacteriol.* **2006**, *188*, 2726–2729. [CrossRef] [PubMed]
126. Zhang, X.; McDaniel, A.D.; Wolf, L.E.; Keusch, G.T.; Waldor, M.K.; Acheson, D.W.K. Quinolone Antibiotics Induce Shiga Toxin-Encoding Bacteriophages, Toxin Production, and Death in Mice. *J. Infect. Dis.* **2000**, *181*, 664–670. [CrossRef]
127. Abeles, S.R.; Ly, M.; Santiago-Rodriguez, T.M.; Pride, D.T. Effects of Long Term Antibiotic Therapy on Human Oral and Fecal Viromes. *PLoS ONE* **2015**, *10*, e0134941. [CrossRef]

128. Modi, S.R.; Lee, H.H.; Spina, C.S.; Collins, J.J. Antibiotic Treatment Expands the Resistance Reservoir and Ecological Network of the Phage Metagenome. *Nature* **2013**, *499*, 219–222. [CrossRef]
129. Sutcliffe, S.G.; Shamash, M.; Hynes, A.P.; Maurice, C.F. Common Oral Medications Lead to Prophage Induction in Bacterial Isolates from the Human Gut. *Viruses* **2021**, *13*, 455. [CrossRef]
130. Sadiq, U.; Shrestha, U.; Guzman, N. Prevention of Opportunistic Infections in HIV/AIDS. In *StatPearls*; StatPearls Publishing: Treasure Island, FL, USA, 2025.
131. Seddon, J.; Bhagani, S. Antimicrobial Therapy for the Treatment of Opportunistic Infections in HIV/AIDS Patients: A Critical Appraisal. *HIV AIDS* **2011**, *3*, 19–33. [CrossRef]
132. Pravitha, B.P.; Prathap, P.; Asokan, N.; Sudhiraj, T.S. The Profile of Sexually Transmitted Infections of Men Who Have Sex with Men: A Tertiary Care Center-Based Comparative Cross-Sectional Study. *Indian J. Sex. Transm. Dis. AIDS* **2023**, *44*, 128–131. [CrossRef]
133. Atkins, K.; Wiginton, J.M.; Carpino, T.; Sanchez, T.H.; Murray, S.M.; Baral, S.D. Transactional Sex, HIV, and Bacterial STIs Among U.S. Men Who Have Sex with Men. *Am. J. Prev. Med.* **2024**, *67*, 722–729. [CrossRef]
134. Men Who Have Sex with Men (MSM). Available online: https://www.cdc.gov/std/treatment-guidelines/msm.htm (accessed on 12 December 2025).
135. DiMarco, D.E.; Urban, M.A.; Vail, R.M.; Shah, S.S.; Fine, S.M.; McGowan, J.P.; Merrick, S.T.; Radix, A.E.; Rodrigues, J.; Norton, B.L.; et al. *Doxycycline Post-Exposure Prophylaxis to Prevent Bacterial Sexually Transmitted Infections*; New York State Department of Health AIDS Institute Clinical Guidelines; Johns Hopkins University: Baltimore, MD, USA, 2024.
136. CDC Doxy PEP for Bacterial STI Prevention. Available online: https://www.cdc.gov/sti/hcp/doxy-pep/index.html (accessed on 12 December 2025).
137. Luetkemeyer, A.F.; Donnell, D.; Dombrowski, J.C.; Cohen, S.; Grabow, C.; Brown, C.E.; Malinski, C.; Perkins, R.; Nasser, M.; Lopez, C.; et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *N. Engl. J. Med.* **2023**, *388*, 1296–1306. [CrossRef]
138. Szondy, I.; Meznerics, F.A.; Lőrincz, K.; Kemény, L.V.; Walter, A.; Mohammed, A.A.; Hegyi, P.; Kiss, N.; Bánvölgyi, A. Doxycycline Prophylaxis for the Prevention of Sexually Transmitted Infections: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Int. J. Infect. Dis.* **2024**, *147*, 107186. [CrossRef]
139. Ramakrishna, C.; Mendonca, S.; Ruegger, P.M.; Kim, J.H.; Borneman, J.; Cantin, E.M. Herpes Simplex Virus Infection, Acyclovir and IVIG Treatment All Independently Cause Gut Dysbiosis. *PLoS ONE* **2020**, *15*, e0237189. [CrossRef]
140. De Paepe, M.; Tournier, L.; Moncaut, E.; Son, O.; Langella, P.; Petit, M.-A. Carriage of λ Latent Virus Is Costly for Its Bacterial Host Due to Frequent Reactivation in Monoxenic Mouse Intestine. *PLoS Genet.* **2016**, *12*, e1005861. [CrossRef] [PubMed]
141. Duerkop, B.A.; Clements, C.V.; Rollins, D.; Rodrigues, J.L.M.; Hooper, L.V. A Composite Bacteriophage Alters Colonization by an Intestinal Commensal Bacterium. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 17621–17626. [CrossRef]
142. Davies, E.V.; James, C.E.; Williams, D.; O'Brien, S.; Fothergill, J.L.; Haldenby, S.; Paterson, S.; Winstanley, C.; Brockhurst, M.A. Temperate Phages Both Mediate and Drive Adaptive Evolution in Pathogen Biofilms. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 8266–8271. [CrossRef]
143. Le-Trilling, V.T.K.; Ebel, J.-F.; Baier, F.; Wohlgemuth, K.; Pfeifer, K.R.; Mookhoek, A.; Krebs, P.; Determann, M.; Katschinski, B.; Adamczyk, A.; et al. Acute Cytomegalovirus Infection Modulates the Intestinal Microbiota and Targets Intestinal Epithelial Cells. *Eur. J. Immunol.* **2023**, *53*, 2249940. [CrossRef] [PubMed]
144. Wang, X.; Sun, L.; Li, P.; Zhang, S. Changes in the Gut Microbiome Can Predict and Decrease Epstein-Barr Virus Infection Risk in Children after Liver Transplantation. *Transplant. Infect. Dis.* **2023**, *25*, e14114. [CrossRef] [PubMed]
145. Fadlallah, S.; Bitar, E.R.; Hussein, H.; Jallad, M.-A.; Matar, G.M.; Rahal, E.A. The Interplay between Epstein-Barr Virus DNA and Gut Microbiota in the Development of Arthritis in a Mouse Model. *Microbiol. Spectr.* **2023**, *11*, e02042-23. [CrossRef]
146. Wen, Y.; Xu, H.; Han, J.; Jin, R.; Chen, H. How Does Epstein–Barr Virus Interact with Other Microbiomes in EBV-Driven Cancers? *Front. Cell. Infect. Microbiol.* **2022**, *12*, 852066. [CrossRef]
147. Brun, P.; Qesari, M.; Marconi, P.C.; Kotsafti, A.; Porzionato, A.; Macchi, V.; Schwendener, R.A.; Scarpa, M.; Giron, M.C.; Palù, G.; et al. Herpes Simplex Virus Type 1 Infects Enteric Neurons and Triggers Gut Dysfunction via Macrophage Recruitment. *Front. Cell. Infect. Microbiol.* **2018**, *8*, 74. [CrossRef]
148. Brun, P.; Conti, J.; Zatta, V.; Russo, V.; Scarpa, M.; Kotsafti, A.; Porzionato, A.; De Caro, R.; Scarpa, M.; Fassan, M.; et al. Persistent Herpes Simplex Virus Type 1 Infection of Enteric Neurons Triggers CD8+ T Cell Response and Gastrointestinal Neuromuscular Dysfunction. *Front. Cell. Infect. Microbiol.* **2021**, *11*, 615350. [CrossRef]
149. Padhi, P.; Worth, C.; Zenitsky, G.; Jin, H.; Sambamurti, K.; Anantharam, V.; Kanthasamy, A.; Kanthasamy, A.G. Mechanistic Insights into Gut Microbiome Dysbiosis-Mediated Neuroimmune Dysregulation and Protein Misfolding and Clearance in the Pathogenesis of Chronic Neurodegenerative Disorders. *Front. Neurosci.* **2022**, *16*, 836605. [CrossRef]

150. Amador-Molina, A.; Hernández-Valencia, J.F.; Lamoyi, E.; Contreras-Paredes, A.; Lizano, M. Role of Innate Immunity against Human Papillomavirus (HPV) Infections and Effect of Adjuvants in Promoting Specific Immune Response. *Viruses* **2013**, *5*, 2624–2642. [CrossRef]
151. Baj, J.; Forma, A.; Dudek, I.; Chilimoniuk, Z.; Dobosz, M.; Dobrzyński, M.; Teresiński, G.; Buszewicz, G.; Flieger, J.; Portincasa, P. The Involvement of Human Papilloma Virus in Gastrointestinal Cancers. *Cancers* **2022**, *14*, 2607. [CrossRef]
152. Black, A.P.B.; Ardern-Jones, M.R.; Kasprowicz, V.; Bowness, P.; Jones, L.; Bailey, A.S.; Ogg, G.S. Human Keratinocyte Induction of Rapid Effector Function in Antigen-Specific Memory CD4+ and CD8+ T Cells. *Eur. J. Immunol.* **2007**, *37*, 1485–1493. [CrossRef] [PubMed]
153. Lebre, M.C.; van der Aar, A.M.G.; van Baarsen, L.; van Capel, T.M.M.; Schuitemaker, J.H.N.; Kapsenberg, M.L.; de Jong, E.C. Human Keratinocytes Express Functional Toll-Like Receptor 3, 4, 5, and 9. *J. Investig. Dermatol.* **2007**, *127*, 331–341. [CrossRef] [PubMed]
154. Miller, L.S.; Modlin, R.L. Human Keratinocyte Toll-like Receptors Promote Distinct Immune Responses. *J. Investig. Dermatol.* **2007**, *127*, 262–263. [CrossRef]
155. Ressing, M.E.; van Gent, M.; Gram, A.M.; Hooykaas, M.J.G.; Piersma, S.J.; Wiertz, E.J.H.J. Immune Evasion by Epstein-Barr Virus. In *Epstein Barr Virus Volume 2: One Herpes Virus: Many Diseases*; Münz, C., Ed.; Springer International Publishing: Cham, Switzerland, 2015; pp. 355–381.
156. Silva, J.d.M.; Alves, C.E.d.C.; Pontes, G.S. Epstein-Barr Virus: The Mastermind of Immune Chaos. *Front. Immunol.* **2024**, *15*, 1297994. [CrossRef]
157. Hu, L.; Zhu, T.; Long, J.; Luo, Q.; Lyu, X. From Infection to Immune Exhaustion: The Epstein-Barr Virus and Its Contribution to Immunosenescence. *Biochim. Biophys. Acta (BBA)—Rev. Cancer* **2025**, *1880*, 189421. [CrossRef]
158. Yuan, L.; Zhong, L.; Krummenacher, C.; Zhao, Q.; Zhang, X. Epstein–Barr Virus-Mediated Immune Evasion in Tumor Promotion. *Trends Immunol.* **2025**, *46*, 386–402. [CrossRef]
159. Albanese, M.; Tagawa, T.; Hammerschmidt, W. Strategies of Epstein-Barr Virus to Evade Innate Antiviral Immunity of Its Human Host. *Front. Microbiol.* **2022**, *13*, 955603. [CrossRef]
160. Bhattarai, N.; Rydze, R.T.; Chivero, E.T.; Stapleton, J.T. GB Virus C Viremia Is Associated with Higher Levels of Double-Negative T Cells and Lower T-Cell Activation in HIV-Infected Individuals Receiving Antiretroviral Therapy. *J. Infect. Dis.* **2012**, *206*, 1469–1472. [CrossRef]
161. Liou, S.; Boggavarapu, R.; Cohen, N.R.; Zhang, Y.; Sharma, I.; Zeheb, L.; Mukund Acharekar, N.; Rodgers, H.D.; Islam, S.; Pitts, J.; et al. Structure of Anellovirus-like Particles Reveal a Mechanism for Immune Evasion. *Nat. Commun.* **2024**, *15*, 7219. [CrossRef]
162. Nokhova, A.R.; Elfimov, K.A.; Shestopalov, A.M.; Gashnikova, N.M.; Kurskaya, O.G. Anelloviruses: From General Biology to Their Role as Biomarkers of Immune Competence in HIV Infection. *Viruses* **2026**, *18*, 235. [CrossRef]
163. Brüssow, H.; Canchaya, C.; Hardt, W.-D. Phages and the Evolution of Bacterial Pathogens: From Genomic Rearrangements to Lysogenic Conversion. *Microbiol. Mol. Biol. Rev.* **2004**, *68*, 560–602. [CrossRef]
164. Fortier, L.-C.; Sekulovic, O. Importance of Prophages to Evolution and Virulence of Bacterial Pathogens. *Virulence* **2013**, *4*, 354–365. [CrossRef]
165. Haaber, J.; Leisner, J.J.; Cohn, M.T.; Catalan-Moreno, A.; Nielsen, J.B.; Westh, H.; Penadés, J.R.; Ingmer, H. Bacterial Viruses Enable Their Host to Acquire Antibiotic Resistance Genes from Neighbouring Cells. *Nat. Commun.* **2016**, *7*, 13333. [CrossRef]
166. Whitehurst, C.B.; Rizk, M.; Teklezghi, A.; Spagnuolo, R.A.; Pagano, J.S.; Wahl, A. HIV Co-Infection Augments EBV-Induced Tumorigenesis in Vivo. *Front. Virol.* **2022**, *2*, 861628. [CrossRef] [PubMed]
167. Grogg, K.L.; Miller, R.F.; Dogan, A. HIV Infection and Lymphoma. *J. Clin. Pathol.* **2007**, *60*, 1365–1372. [CrossRef] [PubMed]
168. Looker, K.J.; Elmes, J.A.R.; Gottlieb, S.L.; Schiffer, J.T.; Vickerman, P.; Turner, K.M.E.; Boily, M.-C. Effect of HSV-2 Infection on Subsequent HIV Acquisition: An Updated Systematic Review and Meta-Analysis. *Lancet Infect. Dis.* **2017**, *17*, 1303–1316. [CrossRef]
169. Van de Perre, P.; Segondy, M.; Foulongne, V.; Ouedraogo, A.; Konate, I.; Huraux, J.-M.; Mayaud, P.; Nagot, N. Herpes Simplex Virus and HIV-1: Deciphering Viral Synergy. *Lancet Infect. Dis.* **2008**, *8*, 490–497. [CrossRef]
170. Cunningham, A.L.; Turner, R.R.; Miller, A.C.; Para, M.F.; Merigan, T.C. Evolution of Recurrent Herpes Simplex Lesions. An Immunohistologic Study. *J. Clin. Investig.* **1985**, *75*, 226–233. [CrossRef]
171. Koelle, D.M.; Abbo, H.; Peck, A.; Ziegweid, K.; Corey, L. Direct Recovery of Herpes Simplex Virus (HSV)-Specific T Lymphocyte Clones from Recurrent Genital HSV-2 Lesions. *J. Infect. Dis.* **1994**, *169*, 956–961. [CrossRef]
172. Noguera-Julian, M.; Rocafort, M.; Guillén, Y.; Rivera, J.; Casadellà, M.; Nowak, P.; Hildebrand, F.; Zeller, G.; Parera, M.; Bellido, R.; et al. Gut Microbiota Linked to Sexual Preference and HIV Infection. *eBioMedicine* **2016**, *5*, 135–146. [CrossRef]
173. Lin, H.; Chen, Y.; Abror-Lacks, G.; Price, M.; Morris, A.; Sun, J.; Palella, F.; Chew, K.W.; Brown, T.T.; Rinaldo, C.R.; et al. Sexual Behavior Is Linked to Changes in Gut Microbiome and Systemic Inflammation That Lead to HIV-1 Infection in Men Who Have Sex with Men. *Commun. Biol.* **2024**, *7*, 1145. [CrossRef] [PubMed]

174. Rametse, C.L.; Adefuye, A.O.; Olivier, A.J.; Curry, L.; Gamieldien, H.; Burgers, W.A.; Lewis, D.A.; Williamson, A.-L.; Katz, A.A.; Passmore, J.-A.S. Inflammatory Cytokine Profiles of Semen Influence Cytokine Responses of Cervicovaginal Epithelial Cells. *Front. Immunol.* **2018**, *9*, 2721. [CrossRef] [PubMed]
175. Monaco, C.L.; Gootenberg, D.B.; Zhao, G.; Handley, S.A.; Ghebremichael, M.S.; Lim, E.S.; Lankowski, A.; Baldridge, M.T.; Wilen, C.B.; Flagg, M.; et al. Altered Virome and Bacterial Microbiome in Human Immunodeficiency Virus-Associated Acquired Immunodeficiency Syndrome. *Cell Host Microbe* **2016**, *19*, 311–322. [CrossRef]
176. Li, K.; Deng, J.; Zhang, C.; Lai, G.; Xie, B.; Zhong, X. Gut Microbiome Dysbiosis in Men Who Have Sex with Men Increases HIV Infection Risk through Immunity Homeostasis Alteration. *Front. Cell. Infect. Microbiol.* **2023**, *13*, 1260068. [CrossRef] [PubMed]
177. Ackerley, C.G.; Smith, S.A.; Murray, P.M.; Amancha, P.K.; Arthur, R.A.; Zhu, Z.; Chahroudi, A.; Amara, R.R.; Hu, Y.-J.; Kelley, C.F. The Rectal Mucosal Immune Environment and HIV Susceptibility among Young Men Who Have Sex with Men. *Front. Immunol.* **2022**, *13*, 972170. [CrossRef]
178. Chen, Y.; Lin, H.; Cole, M.; Morris, A.; Martinson, J.; Mckay, H.; Mimiaga, M.; Margolick, J.; Fitch, A.; Methe, B.; et al. Signature Changes in Gut Microbiome Are Associated with Increased Susceptibility to HIV-1 Infection in MSM. *Microbiome* **2021**, *9*, 237. [CrossRef]
179. Pescatore, N.A.; Pollak, R.; Kraft, C.S.; Mulle, J.G.; Kelley, C.F. Short Communication: Anatomic Site of Sampling and the Rectal Mucosal Microbiota in HIV Negative Men Who Have Sex with Men Engaging in Condomless Receptive Anal Intercourse. *AIDS Res. Hum. Retroviruses* **2018**, *34*, 277–281. [CrossRef]
180. Goddard, S.L.; Poynten, I.M.; Petoumenos, K.; Jin, F.; Hillman, R.J.; Law, C.; Roberts, J.M.; Fairley, C.K.; Garland, S.M.; Grulich, A.E.; et al. Self-Reported Anal Symptoms and Their Association with Anal Pathology among Gay and Bisexual Men: A Cross-Sectional Observational Analysis. *Sex. Health* **2021**, *18*, 123–129. [CrossRef]
181. Owen, W.F. Sexually Transmitted Diseases and Traumatic Problems in Homosexual Men. *Ann. Intern. Med.* **1980**, *92*, 805–808. [CrossRef]
182. Liu, C.M.; Hungate, B.A.; Tobian, A.A.R.; Ravel, J.; Prodger, J.L.; Serwadda, D.; Kigozi, G.; Galiwango, R.M.; Nalugoda, F.; Keim, P.; et al. Penile Microbiota and Female Partner Bacterial Vaginosis in Rakai, Uganda. *mBio* **2015**, *6*, e00589-15. [CrossRef]
183. Zozaya, M.; Ferris, M.J.; Siren, J.D.; Lillis, R.; Myers, L.; Nsuami, M.J.; Eren, A.M.; Brown, J.; Taylor, C.M.; Martin, D.H. Bacterial Communities in Penile Skin, Male Urethra, and Vaginas of Heterosexual Couples with and without Bacterial Vaginosis. *Microbiome* **2016**, *4*, 16. [CrossRef] [PubMed]
184. Eren, A.M.; Zozaya, M.; Taylor, C.M.; Dowd, S.E.; Martin, D.H.; Ferris, M.J. Exploring the Diversity of Gardnerella Vaginalis in the Genitourinary Tract Microbiota of Monogamous Couples Through Subtle Nucleotide Variation. *PLoS ONE* **2011**, *6*, e26732. [CrossRef] [PubMed]
185. Tuddenham, S.; Ravel, J.; Marrazzo, J.M. Protection and Risk: Male and Female Genital Microbiota and Sexually Transmitted Infections. *J. Infect. Dis.* **2021**, *223*, S222–S235. [CrossRef]
186. Rocafort, M.; Gootenberg, D.B.; Luévano, J.M.; Paer, J.M.; Hayward, M.R.; Bramante, J.T.; Ghebremichael, M.S.; Xu, J.; Rogers, Z.H.; Munoz, A.R.; et al. HIV-Associated Gut Microbial Alterations Are Dependent on Host and Geographic Context. *Nat. Commun.* **2024**, *15*, 1055. [CrossRef]
187. Li, S.X.; Armstrong, A.J.S.; Neff, C.P.; Shaffer, M.; Lozupone, C.A.; Palmer, B.E. Complexities of Gut Microbiome Dysbiosis in the Context of HIV Infection and Antiretroviral Therapy. *Clin. Pharmacol. Ther.* **2016**, *99*, 600–611. [CrossRef]
188. Mehandru, S.; Poles, M.A.; Tenner-Racz, K.; Horowitz, A.; Hurley, A.; Hogan, C.; Boden, D.; Racz, P.; Markowitz, M. Primary HIV-1 Infection Is Associated with Preferential Depletion of CD4+ T Lymphocytes from Effector Sites in the Gastrointestinal Tract. *J. Exp. Med.* **2004**, *200*, 761–770. [CrossRef]
189. Brenchley, J.M.; Paiardini, M.; Knox, K.S.; Asher, A.I.; Cervasi, B.; Asher, T.E.; Scheinberg, P.; Price, D.A.; Hage, C.A.; Kholi, L.M.; et al. Differential Th17 CD4 T-Cell Depletion in Pathogenic and Nonpathogenic Lentiviral Infections. *Blood* **2008**, *112*, 2826–2835. [CrossRef]
190. Liang, S.C.; Tan, X.-Y.; Luxenberg, D.P.; Karim, R.; Dunussi-Joannopoulos, K.; Collins, M.; Fouser, L.A. Interleukin (IL)-22 and IL-17 Are Coexpressed by Th17 Cells and Cooperatively Enhance Expression of Antimicrobial Peptides. *J. Exp. Med.* **2006**, *203*, 2271–2279. [CrossRef] [PubMed]
191. Dillon, S.M.; Manuzak, J.A.; Leone, A.K.; Lee, E.J.; Rogers, L.M.; McCarter, M.D.; Wilson, C.C. HIV-1 Infection of Human Intestinal Lamina Propria CD4+ T Cells in Vitro Is Enhanced by Exposure to Commensal *Escherichia coli*. *J. Immunol.* **2012**, *189*, 885–896. [CrossRef] [PubMed]
192. Allers, K.; Loddenkemper, C.; Hofmann, J.; Unbehaun, A.; Kunkel, D.; Moos, V.; Kaup, F.-J.; Stahl-Hennig, C.; Sauermann, U.; Epple, H.-J.; et al. Gut Mucosal FOXP3+ Regulatory CD4+ T Cells and Nonregulatory CD4+ T Cells Are Differentially Affected by Simian Immunodeficiency Virus Infection in Rhesus Macaques. *J. Virol.* **2010**, *84*, 3259–3269. [CrossRef] [PubMed]
193. Jiao, Y.; Fu, J.; Xing, S.; Fu, B.; Zhang, Z.; Shi, M.; Wang, X.; Zhang, J.; Jin, L.; Kang, F.; et al. The Decrease of Regulatory T Cells Correlates with Excessive Activation and Apoptosis of CD8+ T Cells in HIV-1-Infected Typical Progressors, but Not in Long-Term Non-Progressors. *Immunology* **2009**, *128*, e366–e375. [CrossRef]

194. Paiardini, M.; Müller-Trutwin, M. HIV-Associated Chronic Immune Activation. *Immunol. Rev.* **2013**, *254*, 78–101. [CrossRef]
195. Meng, Q.; Xu, L.; Xu, F.; Shen, X.; Yue, J. HIV-Associated Gut Dysbiosis Drives Oncogenesis through Metabolic-Immune Crosstalk: Mechanisms and Therapeutic Implications. *Front. Oncol.* **2025**, *15*, 1634388. [CrossRef]
196. Monaco, C.L. HIV, AIDS, and the Virome: Gut Reactions. *Cell Host Microbe* **2022**, *30*, 466–470. [CrossRef]
197. Villoslada-Blanco, P.; Pérez-Matute, P.; Íñiguez, M.; Recio-Fernández, E.; Blanco-Navarrete, P.; Metola, L.; Ibarra, V.; Alba, J.; de Toro, M.; Oteo, J.A. Integrase Inhibitors Partially Restore Bacterial Translocation, Inflammation and Gut Permeability Induced by HIV Infection: Impact on Gut Microbiota. *Infect. Dis. Ther.* **2022**, *11*, 1541–1557. [CrossRef]
198. Liu, K.; Li, Y.; Xu, R.; Zhang, Y.; Zheng, C.; Wan, Z.; Li, H.; Yang, Z.; Jin, X.; Hao, P.; et al. HIV-1 Infection Alters the Viral Composition of Plasma in Men Who Have Sex with Men. *mSphere* **2021**, *6*, e00081-21. [CrossRef]
199. Chris, D.M.; Jesper, E.-O.; Ole, K.; Jan, P.; Jens, K.C.; Marie, S.B.; Jens, O.N.; Kim, K. TTV Viral Load As a Marker for Immune Reconstitution After Initiation of HAART in HIV-Infected Patients. *HIV Clin. Trials* **2002**, *3*, 287–295. [CrossRef] [PubMed]
200. Esser, P.L.; Quintanares, G.H.R.; Langhans, B.; Heger, E.; Böhm, M.; Jensen, B.-E.O.L.E.; Esser, S.; Lübke, N.; Fätkenheuer, G.; Lengauer, T.; et al. Torque Teno Virus Load Is Associated with Centers for Disease Control and Prevention Stage and CD4+ Cell Count in People Living with Human Immunodeficiency Virus but Seems Unrelated to AIDS-Defining Events and Human Pegivirus Load. *J. Infect. Dis.* **2024**, *230*, e437–e446. [CrossRef]
201. Wei, F.; Gaisa, M.M.; D'Souza, G.; Xia, N.; Giuliano, A.R.; Hawes, S.E.; Gao, L.; Cheng, S.-H.; Donà, M.G.; Goldstone, S.E.; et al. Epidemiology of Anal Human Papillomavirus Infection and High-Grade Squamous Intraepithelial Lesions in 29 900 Men According to HIV Status, Sexuality, and Age: A Collaborative Pooled Analysis of 64 Studies. *Lancet HIV* **2021**, *8*, e531–e543. [CrossRef] [PubMed]
202. Donà, M.G.; Gheit, T.; Latini, A.; Benevolo, M.; Torres, M.; Smelov, V.; McKay-Chopin, S.; Giglio, A.; Cristaudo, A.; Zaccarelli, M.; et al. Alpha, Beta and Gamma Human Papillomaviruses in the Anal Canal of HIV-Infected and Uninfected Men Who Have Sex with Men. *J. Infect.* **2015**, *71*, 74–84. [CrossRef]
203. Palefsky, J. Human Papillomavirus-Related Disease in People with HIV. *Curr. Opin. HIV AIDS* **2009**, *4*, 52–56. [CrossRef]
204. Yunihastuti, E.; Teeratakulpisarn, N.; Jeo, W.S.; Nilasari, H.; Rachmadi, L.; Somia, I.K.A.; Sukmawati, M.D.D.; Amijaya, K.A.T.; Yee, I.A.; Hairunisa, N.; et al. Incidence, Clearance, Persistence and Factors Related with High-Risk Anal HPV Persistence in South-East Asian MSM and Transgender Women. *AIDS* **2020**, *34*, 1933–1941. [CrossRef]
205. Lecuit, M.; Eloit, M. The Human Virome: New Tools and Concepts. *Trends Microbiol.* **2013**, *21*, 510–515. [CrossRef]
206. Rascovan, N.; Duraisamy, R.; Desnues, C. Metagenomics and the Human Virome in Asymptomatic Individuals. *Annu. Rev. Microbiol.* **2016**, *70*, 125–141. [CrossRef]
207. Villoslada-Blanco, P.; Pérez-Matute, P.; Íñiguez, M.; Recio-Fernández, E.; Jansen, D.; De Coninck, L.; Close, L.; Blanco-Navarrete, P.; Metola, L.; Ibarra, V.; et al. Impact of HIV Infection and Integrase Strand Transfer Inhibitors-Based Treatment on the Gut Virome. *Sci. Rep.* **2022**, *12*, 21658. [CrossRef] [PubMed]
208. Lucke, K.; Miehlke, S.; Jacobs, E.; Schuppler, M. Prevalence of Bacteroides and Prevotella Spp. in Ulcerative Colitis. *J. Med. Microbiol.* **2006**, *55*, 617–624. [CrossRef]
209. Hunt, P.W.; Martin, J.N.; Sinclair, E.; Epling, L.; Teague, J.; Jacobson, M.A.; Tracy, R.P.; Corey, L.; Deeks, S.G. Valganciclovir Reduces T Cell Activation in HIV-Infected Individuals with Incomplete CD4+ T Cell Recovery on Antiretroviral Therapy. *J. Infect. Dis.* **2011**, *203*, 1474–1483. [CrossRef] [PubMed]
210. Steininger, C.; Puchhammer-Stöckl, E.; Popow-Kraupp, T. Cytomegalovirus Disease in the Era of Highly Active Antiretroviral Therapy (HAART). *J. Clin. Virol.* **2006**, *37*, 1–9. [CrossRef]
211. Emery, V. Investigation of CMV Disease in Immunocompromised Patients. *J. Clin. Pathol.* **2001**, *54*, 84–88. [CrossRef] [PubMed]
212. Sylwester, A.W.; Mitchell, B.L.; Edgar, J.B.; Taormina, C.; Pelte, C.; Ruchti, F.; Sleath, P.R.; Grabstein, K.H.; Hosken, N.A.; Kern, F.; et al. Broadly Targeted Human Cytomegalovirus-Specific CD4+ and CD8+ T Cells Dominate the Memory Compartments of Exposed Subjects. *J. Exp. Med.* **2005**, *202*, 673–685. [CrossRef] [PubMed]
213. Laichalk, L.L.; Hochberg, D.; Babcock, G.J.; Freeman, R.B.; Thorley-Lawson, D.A. The Dispersal of Mucosal Memory B Cells: Evidence from Persistent EBV Infection. *Immunity* **2002**, *16*, 745–754. [CrossRef]
214. Verdu-Bou, M.; Tapia, G.; Hernandez-Rodriguez, A.; Navarro, J.-T. Clinical and Therapeutic Implications of Epstein–Barr Virus in HIV-Related Lymphomas. *Cancers* **2021**, *13*, 5534. [CrossRef]
215. Patel, P.; Bush, T.; Mayer, K.H.; Desai, S.; Henry, K.; Overton, E.T.; Conley, L.; Hammer, J.; Brooks, J.T. Prevalence and Risk Factors Associated with Herpes Simplex Virus-2 Infection in a Contemporary Cohort of HIV-Infected Persons in the United States. *Sex. Transm. Dis.* **2012**, *39*, 154–160. [CrossRef]
216. Smit, C.; Pfrommer, C.; Mindel, A.; Taylor, J.; Spaargaren, J.; Berkhout, B.; Coutinho, R.; Dukers, N.H.T.M. Rise in Seroprevalence of Herpes Simplex Virus Type 1 among Highly Sexual Active Homosexual Men and an Increasing Association between Herpes Simplex Virus Type 2 and HIV over Time (1984–2003). *Eur. J. Epidemiol.* **2007**, *22*, 937–944. [CrossRef]
217. Posavad, C.M.; Wald, A.; Kuntz, S.; Huang, M.L.; Selke, S.; Krantz, E.; Corey, L. Frequent Reactivation of Herpes Simplex Virus among HIV-1-Infected Patients Treated with Highly Active Antiretroviral Therapy. *J. Infect. Dis.* **2004**, *190*, 693–696. [CrossRef]

218. Tobian, A.A.R.; Grabowski, M.K.; Serwadda, D.; Newell, K.; Ssebbowa, P.; Franco, V.; Nalugoda, F.; Wawer, M.J.; Gray, R.H.; Quinn, T.C.; et al. Reactivation of Herpes Simplex Virus Type 2 After Initiation of Antiretroviral Therapy. *J. Infect. Dis.* **2013**, *208*, 839–846. [CrossRef] [PubMed]
219. Yang, Q.; Ouyang, J.; Sun, F.; Yang, J. Short-Chain Fatty Acids: A Soldier Fighting Against Inflammation and Protecting from Tumorigenesis in People with Diabetes. *Front. Immunol.* **2020**, *11*, 590685. [CrossRef]
220. Parada Venegas, D.; De la Fuente, M.K.; Landskron, G.; González, M.J.; Quera, R.; Dijkstra, G.; Harmsen, H.J.M.; Faber, K.N.; Hermoso, M.A. Corrigendum: Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. *Front. Immunol.* **2019**, *10*, 1486. [CrossRef]
221. Simms-Waldrip, T.R.; Sunkersett, G.; Coughlin, L.A.; Savani, M.R.; Arana, C.; Kim, J.; Kim, M.; Zhan, X.; Greenberg, D.E.; Xie, Y.; et al. Antibiotic-Induced Depletion of Anti-Inflammatory Clostridia Is Associated with the Development of Graft-versus-Host Disease in Pediatric Stem Cell Transplantation Patients. *Biol. Blood Marrow Transplant.* **2017**, *23*, 820–829. [CrossRef]
222. Biagi, E.; Zama, D.; Nastasi, C.; Consolandi, C.; Fiori, J.; Rampelli, S.; Turroni, S.; Centanni, M.; Severgnini, M.; Peano, C.; et al. Gut Microbiota Trajectory in Pediatric Patients Undergoing Hematopoietic SCT. *Bone Marrow Transplant.* **2015**, *50*, 992–998. [CrossRef]
223. Peled, J.U.; Devlin, S.M.; Staffas, A.; Lumish, M.; Khanin, R.; Littmann, E.R.; Ling, L.; Kosuri, S.; Maloy, M.; Slingerland, J.B.; et al. Intestinal Microbiota and Relapse After Hematopoietic-Cell Transplantation. *J. Clin. Oncol.* **2017**, *35*, 1650–1659. [CrossRef]
224. Jenq, R.R.; Ubeda, C.; Taur, Y.; Menezes, C.C.; Khanin, R.; Dudakov, J.A.; Liu, C.; West, M.L.; Singer, N.V.; Equinda, M.J.; et al. Regulation of Intestinal Inflammation by Microbiota Following Allogeneic Bone Marrow Transplantation. *J. Exp. Med.* **2012**, *209*, 903–911. [CrossRef] [PubMed]
225. Biagi, E.; Zama, D.; Rampelli, S.; Turroni, S.; Brigidi, P.; Consolandi, C.; Severgnini, M.; Picotti, E.; Gasperini, P.; Merli, P.; et al. Early Gut Microbiota Signature of aGvHD in Children given Allogeneic Hematopoietic Cell Transplantation for Hematological Disorders. *BMC Med. Genom.* **2019**, *12*, 49. [CrossRef] [PubMed]
226. Fang, P.; Kazmi, S.A.; Jameson, K.G.; Hsiao, E.Y. The Microbiome as a Modifier of Neurodegenerative Disease Risk. *Cell Host Microbe* **2020**, *28*, 201–222. [CrossRef]
227. Kops, N.L.; Eidt, G.; Martins, R.S.; de Miranda, G.P.; Camargo, T.R.; Aqua, C.B.D.; Pinheiro, B.H.G.; de Brito, E.S.; Bandeira, I.C.; Junior, P.R.D.; et al. Prevalence and Correlates of Anal HPV Infection among Men Who Have Sex with Men in Brazil: A Respondent-Driven Sampling Study. *Int. J. Infect. Dis.* **2026**, *163*, 108292. [CrossRef]
228. Deshmukh, A.A.; Damgacioglu, H.; Georges, D.; Sonawane, K.; Clifford, G.M. Human Papillomavirus-Associated Anal Cancer Incidence and Burden Among US Men, According to Sexual Orientation, Human Immunodeficiency Virus Status, and Age. *Clin. Infect. Dis.* **2023**, *77*, 419–424. [CrossRef]
229. Tadese, B.K.; You, X.; Ndao, T.; Tota, J.E.; Chen, Y.-T.; Chowdhary, A.; Pan, J.; Costa, A.C.; Mugo, N. The Burden of HPV Infections and HPV-Related Diseases Among People with HIV: A Systematic Literature Review. *J. Med. Virol.* **2025**, *97*, e70274. [CrossRef]
230. Donà, M.G.; Giuliani, M.; Rollo, F.; Vescio, M.F.; Benevolo, M.; Giglio, A.; Giuliani, E.; Morrone, A.; Latini, A. Incidence and Clearance of Anal High-Risk Human Papillomavirus Infection and Their Risk Factors in Men Who Have Sex with Men Living with HIV. *Sci. Rep.* **2022**, *12*, 184. [CrossRef]
231. Sims, T.T.; Colbert, L.E.; Klopp, A.H. The Role of the Cervicovaginal and Gut Microbiome in Cervical Intraepithelial Neoplasia and Cervical Cancer. *J. Immunother. Precis. Oncol.* **2020**, *4*, 72–78. [CrossRef]
232. Pai, H.D.; Baid, R.; Palshetkar, N.P.; Pai, R.; Pai, A.; Palshetkar, R. Role of Vaginal and Gut Microbiota in Human Papillomavirus (HPV) Progression and Cervical Cancer: A Systematic Review of Microbial Diversity and Probiotic Interventions. *Cureus* **2025**, *17*, e85880. [CrossRef] [PubMed]
233. Leon-Gomez, P.; Romero, V.I. Human Papillomavirus, Vaginal Microbiota and Metagenomics: The Interplay between Development and Progression of Cervical Cancer. *Front. Microbiol.* **2025**, *15*, 1515258. [CrossRef]
234. Mitra, A.; MacIntyre, D.A.; Marchesi, J.R.; Lee, Y.S.; Bennett, P.R.; Kyrgiou, M. The Vaginal Microbiota, Human Papillomavirus Infection and Cervical Intraepithelial Neoplasia: What Do We Know and Where Are We Going Next? *Microbiome* **2016**, *4*, 58. [CrossRef]
235. Lebeau, A.; Bruyere, D.; Roncarati, P.; Peixoto, P.; Hervouet, E.; Cobraiville, G.; Taminiau, B.; Masson, M.; Gallego, C.; Mazzucchelli, G.; et al. HPV Infection Alters Vaginal Microbiome through Down-Regulating Host Mucosal Innate Peptides Used by Lactobacilli as Amino Acid Sources. *Nat. Commun.* **2022**, *13*, 1076. [CrossRef] [PubMed]
236. Vyshenska, D.; Lam, K.C.; Shulzhenko, N.; Morgun, A. Interplay between Viruses and Bacterial Microbiota in Cancer Development. *Semin. Immunol.* **2017**, *32*, 14–24. [CrossRef]
237. Wang, Y.; Thakur, R.; Shen, Q.; He, Y.; Chen, C. Influences of Vaginal Microbiota on Human Papillomavirus Infection and Host Immune Regulation: What We Have Learned? *Decod. Infect. Transm.* **2023**, *1*, 100002. [CrossRef]
238. Colbert, L.E.; Medrano, A.Y.D.; Mikkelson, M.D.; Previs, R.; Eifel, P.J.; Jhingran, A.; Ramondetta, L.; Futreal, P.A.; Jazaeri, A.; Frumovitz, M.; et al. Clonal Expansion of Antigen Specific T-Cells during Radiation Therapy for HPV Associated Cervical Cancers Is Regulated by the Vaginal Microbiome. *Int. J. Radiat. Oncol. Biol. Phys.* **2018**, *102*, S24. [CrossRef]

239. Bourlet, T.; Guglielminotti, C.; Evrard, M.; Berthelot, P.; Grattard, F.; Frésard, A.; Lucht, F.R.; Pozzetto, B. Prevalence of GBV-C/Hepatitis G Virus RNA and E2 Antibody among Subjects Infected with Human Immunodeficiency Virus Type 1 after Parenteral or Sexual Exposure. *J. Med. Virol.* **1999**, *58*, 373–377. [CrossRef]
240. Scallan, M.F.; Clutterbuck, D.; Jarvis, L.M.; Scott, G.R.; Simmonds, P. Sexual Transmission of GB Virus C/Hepatitis G Virus. *J. Med. Virol.* **1998**, *55*, 203–208. [CrossRef]
241. Nerurkar, V.R.; Chua, P.K.; Hoffmann, P.R.; Dashwood, W.-M.; Shikuma, C.M.; Yanagihara, R. High Prevalence of GB Virus C/Hepatitis G Virus Infection among Homosexual Men Infected with Human Immunodeficiency Virus Type 1: Evidence for Sexual Transmission. *J. Med. Virol.* **1998**, *56*, 123–127. [CrossRef]
242. George, S.L.; Varmaz, D.; Stapleton, J.T. GB Virus C Replicates in Primary T and B Lymphocytes. *J. Infect. Dis.* **2006**, *193*, 451–454. [CrossRef] [PubMed]
243. Lavoie, G.R.; Fisher, J.F. Receptive Anal Intercourse and HIV Infection. *World J. AIDS* **2017**, *7*, 269–278. [CrossRef]
244. Baggaley, R.F.; White, R.G.; Boily, M.-C. HIV Transmission Risk through Anal Intercourse: Systematic Review, Meta-Analysis and Implications for HIV Prevention. *Int. J. Epidemiol.* **2010**, *39*, 1048–1063. [CrossRef]
245. Tillmann, H.L.; Heiken, H.; Knapik-Botor, A.; Heringlake, S.; Ockenga, J.; Wilber, J.C.; Goergen, B.; Detmer, J.; McMorrow, M.; Stoll, M.; et al. Infection with GB Virus C and Reduced Mortality among HIV-Infected Patients. *N. Engl. J. Med.* **2001**, *345*, 715–724. [CrossRef]
246. Souza, I.E.; Zhang, W.; Diaz, R.S.; Chaloner, K.; Klinzman, D.; Stapleton, J.T. Effect of GB Virus C on Response to Antiretroviral Therapy in HIV-Infected Brazilians. *HIV Med.* **2006**, *7*, 25–31. [CrossRef]
247. Rodriguez, B.; Woolley, I.; Lederman, M.M.; Zdunek, D.; Hess, G.; Valdez, H. Effect of GB Virus C Coinfection on Response to Antiretroviral Treatment in Human Immunodeficiency Virus-Infected Patients. *J. Infect. Dis.* **2003**, *187*, 504–507. [CrossRef] [PubMed]
248. Heringlake, S.; Ockenga, J.; Tillmann, H.L.; Trautwein, C.; Meissner, D.; Stoll, M.; Hunt, J.; Jou, C.; Solomon, N.; Schmidt, R.E.; et al. GB Virus C/Hepatitis G Virus Infection: A Favorable Prognostic Factor in Human Immunodeficiency Virus-Infected Patients? *J. Infect. Dis.* **1998**, *177*, 1723–1726. [CrossRef]
249. Yeo, A.E.; Matsumoto, A.; Hisada, M.; Shih, J.W.; Alter, H.J.; Goedert, J.J. Effect of Hepatitis G Virus Infection on Progression of HIV Infection in Patients with Hemophilia. Multicenter Hemophilia Cohort Study. *Ann. Intern. Med.* **2000**, *132*, 959–963. [CrossRef]
250. Schwarze-Zander, C.; Neibecker, M.; Othman, S.; Tural, C.; Clotet, B.; Blackard, J.T.; Kupfer, B.; Luechters, G.; Chung, R.T.; Rockstroh, J.K.; et al. GB Virus C Coinfection in Advanced HIV Type-1 Disease Is Associated with Low CCR5 and CXCR4 Surface Expression on CD4+ T-Cells. *Antivir. Ther.* **2010**, *15*, 745–752. [CrossRef] [PubMed]
251. Nattermann, J.; Nischalke, H.-D.; Kupfer, B.; Rockstroh, J.; Hess, L.; Sauerbruch, T.; Spengler, U. Regulation of CC Chemokine Receptor 5 in Hepatitis G Virus Infection. *AIDS* **2003**, *17*, 1457–1462. [CrossRef]
252. Xiang, J.; McLinden, J.H.; Chang, Q.; Kaufman, T.M.; Stapleton, J.T. An 85-Aa Segment of the GB Virus Type C NS5A Phosphoprotein Inhibits HIV-1 Replication in CD4+ Jurkat T Cells. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 15570–15575. [CrossRef]
253. Jung, S.; Eichenmüller, M.; Donhauser, N.; Neipel, F.; Engel, A.M.; Hess, G.; Fleckenstein, B.; Reil, H. HIV Entry Inhibition by the Envelope 2 Glycoprotein of GB Virus C. *AIDS* **2007**, *21*, 645–647. [CrossRef] [PubMed]
254. Koedel, Y.; Eissmann, K.; Wend, H.; Fleckenstein, B.; Reil, H. Peptides Derived from a Distinct Region of GB Virus C Glycoprotein E2 Mediate Strain-Specific HIV-1 Entry Inhibition. *J. Virol.* **2011**, *85*, 7037–7047. [CrossRef] [PubMed]
255. Chang, Q.; McLinden, J.H.; Stapleton, J.T.; Sathar, M.A.; Xiang, J. Expression of GB Virus C NS5A Protein from Genotypes 1, 2, 3 and 5 and a 30 Aa NS5A Fragment Inhibit Human Immunodeficiency Virus Type 1 Replication in a CD4+ T-Lymphocyte Cell Line. *J. Gen. Virol.* **2007**, *88*, 3341–3346. [CrossRef]
256. Lalle, E.; Sacchi, A.; Abbate, I.; Vitale, A.; Martini, F.; D'Offizi, G.; Antonucci, G.; Castilletti, C.; Poccia, F.; Capobianchi, M.R. Activation of Interferon Response Genes and of Plasmacytoid Dendritic Cells in HIV-1 Positive Subjects with GB Virus C Co-Infection. *Int. J. Immunopathol. Pharmacol.* **2008**, *21*, 161–171. [CrossRef]
257. Nunnari, G.; Nigro, L.; Palermo, F.; Attanasio, M.; Berger, A.; Doerr, H.W.; Pomerantz, R.J.; Cacopardo, B. Slower Progression of HIV-1 Infection in Persons with GB Virus C Co-Infection Correlates with an Intact T-Helper 1 Cytokine Profile. *Ann. Intern. Med.* **2003**, *139*, 26–30. [CrossRef]
258. Rydze, R.T.; Xiang, J.; McLinden, J.H.; Stapleton, J.T. GB Virus Type C Infection Polarizes T-Cell Cytokine Gene Expression toward a Th1 Cytokine Profile via NS5A Protein Expression. *J. Infect. Dis.* **2012**, *206*, 69–72. [CrossRef] [PubMed]
259. Moenkemeyer, M.; Schmidt, R.E.; Wedemeyer, H.; Tillmann, H.L.; Heiken, H. GBV-C Coinfection Is Negatively Correlated to Fas Expression and Fas-Mediated Apoptosis in HIV-1 Infected Patients. *J. Med. Virol.* **2008**, *80*, 1933–1940. [CrossRef] [PubMed]
260. Bhattarai, N.; Stapleton, J.T. GB Virus C: The Good Boy Virus? *Trends Microbiol.* **2012**, *20*, 124–130. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.