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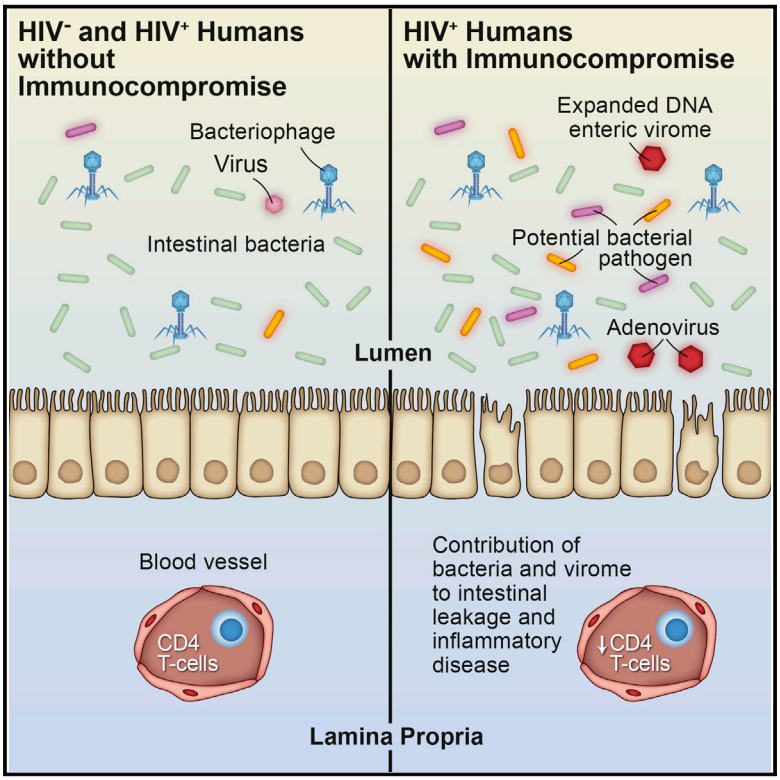
Altered Virome and Bacterial Microbiome in Human Immunodeficiency Virus-Associated Acquired Immunodeficiency Syndrome

Graphical Abstract



Highlights

- In HIV-infected Ugandans, low CD4 T cells were linked to enteric adenovirus expansion
- Low CD4 T cell numbers were also associated with alterations in the bacterial microbiome
- These changes in the virome and bacterial microbiome were independent of ART treatment
- These changes may contribute to AIDS-associated enteropathy and disease progression

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In Brief

Monaco et al. characterize the enteric virome and bacterial microbiome in an HIV-infected Ugandan patient cohort. Low peripheral CD4 T cell counts were associated with an expansion of enteric adenovirus sequences and bacterial microbiome alterations, including increases in Enterobacteriaceae, each of which may contribute to AIDS-associated enteropathy and disease progression.

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Article

Altered Virome and Bacterial Microbiome in Human Immunodeficiency Virus-Associated Acquired Immunodeficiency Syndrome

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SUMMARY

Human immunodeficiency virus (HIV) infection is associated with increased intestinal translocation of microbial products and enteropathy as well as alterations in gut bacterial communities. However, whether the enteric virome contributes to this infection and resulting immunodeficiency remains unknown. We characterized the enteric virome and bacterial microbiome in a cohort of Ugandan patients, including HIV-uninfected or HIV-infected subjects and those either treated with anti-retroviral therapy (ART) or untreated. Low peripheral CD4 T cell counts were associated with an expansion of enteric adenovirus sequences and this increase was independent of ART treatment. Additionally, the enteric bacterial microbiome of patients with lower CD4 T counts exhibited reduced phylogenetic diversity and richness with specific bacteria showing differential abundance, including increases in *Enterobacteriaceae*, which have been associated with inflammation. Thus, immunodeficiency in progressive HIV infection is associated with alterations in the enteric virome and bacterial microbiome, which may contribute to AIDS-associated enteropathy and disease progression.

INTRODUCTION

An estimated 35 million adults worldwide are HIV positive, with the greatest burden of disease in sub-Saharan Africa (Joint United Nations Programme on HIV/AIDS, 2013). HIV infects and depletes CD4 T cells, leading to the development of acquired immunodeficiency syndrome (AIDS), defined by the presence of less than 200 CD4 T cells/μL circulating in the blood (denoted herein as CD4 > 200 or < 200) or the development of an AIDS-defining opportunistic infection or cancer (Selik et al., 2014). Antiretroviral therapy (ART) successfully controls systemic HIV replication but immune recovery is variable (Maartens et al., 2014). A hallmark of HIV disease is a rapid and profound depletion of CD4 T cells in the gut-associated lymphoid tissue (Brenchley et al., 2004; Klatt et al., 2008) and increased translocation of microbial products across this compromised epithelial barrier (Brenchley et al., 2006; Klase et al., 2015). HIV infection can also lead to enteropathy characterized by increased gastrointestinal (GI) inflammation, diarrhea, and malabsorption (Brenchley, 2013). The role of enteric microbes in these disease manifestations is incompletely understood.

The human enteric microbiome contains viruses, bacteria, archaea, fungi, and other eukaryotic organisms (Norman et al., 2014; Virgin, 2014). Enteric human virome and bacterial microbiome alterations have been linked to inflammatory bowel disease (IBD), obesity, and changes in host behavior (Bäckhed et al., 2012; Lyte, 2013; Norman et al., 2015). Enteric eukaryotic viruses can directly affect human health by instigating gastroenteritis, enteritis, or colitis. Bacteriophages can perturb the bacterial community to indirectly influence gut health and may directly interact with the human immune system (Duerkop and Hooper, 2013; Virgin, 2014). In IBD, diversity and richness of the bacterial microbiome is inversely correlated with that of bacteriophages, suggesting an antagonistic relationship between bacteria and bacteriophages during enteric inflammation (Norman et al., 2015). However, little else is known about the contributions of bacteriophages to other human diseases including HIV infection.