The relationship between dietary patterns and the gut virome.

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INTRODUCTION

The gut virome influences disease pathogenesis through interactions with host immunity and phage–host dynamics. Although the effects of diet on bacterial gut microbiota are well established, its impact on the gut virome relatively remains unclear.

HYPOTHESIS

We hypothesize that dietary patterns shape the composition of whole gut communities through interactions with both gut bacteria and viruses.

METHODS

- Metagenomic (MGX) profiles were generated from fecal samples of healthy participants in the MICRObiome Among Nurses (Micro-N), Mind Body Study (MBS), and Men's Lifestyle Validation Study (MLVS) (1989 – 2020).
- Viral taxonomic profiling was performed using BAQLaVa (Bioinformatic Application for Quantification and Labeling of Viral taxonomy).
- Dietary intake was assessed using food frequency questionnaires every four years. [1]
- Ten dietary pattern scores were calculated.

Healthy dietary patterns	Unhealthy dietary patterns
○ Alternative Healthy Eating Index (AHEI)	○ Unhealthy PDI (uPDI)
○ Dietary Approaches to Stop Hypertension (DASH)	○ Empirical Dietary Inflammatory Pattern (EDIP)
○ Alternate Mediterranean Diet Score (aMED)	○ ultra-processed foods (UPF; servings/day)
○ Plant-based Diet Index (PDI)	○ Western diet
○ Healthy PDI (hPDI)	
○ Prudent diet	

- Multivariable linear models adjusted for age, sex, body mass index, diabetes status, physical activity, calorie intake, and sequencing depth were fitted using MaAsLin 3 to identify viral and bacterial taxa associated with dietary patterns. [2]
- Host-phage prediction was performed using iPHoP, an integrated machine learning framework for virus–host assignment. [3]

REFERENCES

1. Jensen JSL, et al., bioRxiv, 2026.
2. Nickols WA, et al., Nat Methods, 2026.
3. Roux S, et al., PLoS Biol, 2023.

RESULTS

- A total of 1,016 participants with 2,236 fecal samples were included in the analysis.
- Greater adherence to healthier diet patterns were associated with increased alpha diversity. Beta diversity differed significantly across dietary patterns (PERMANOVA p = 0.001), although effect sizes were modest (R^2 = 0.13–0.27%).
- A total of 263 viral species, including known and uncultivated taxa were assessed.

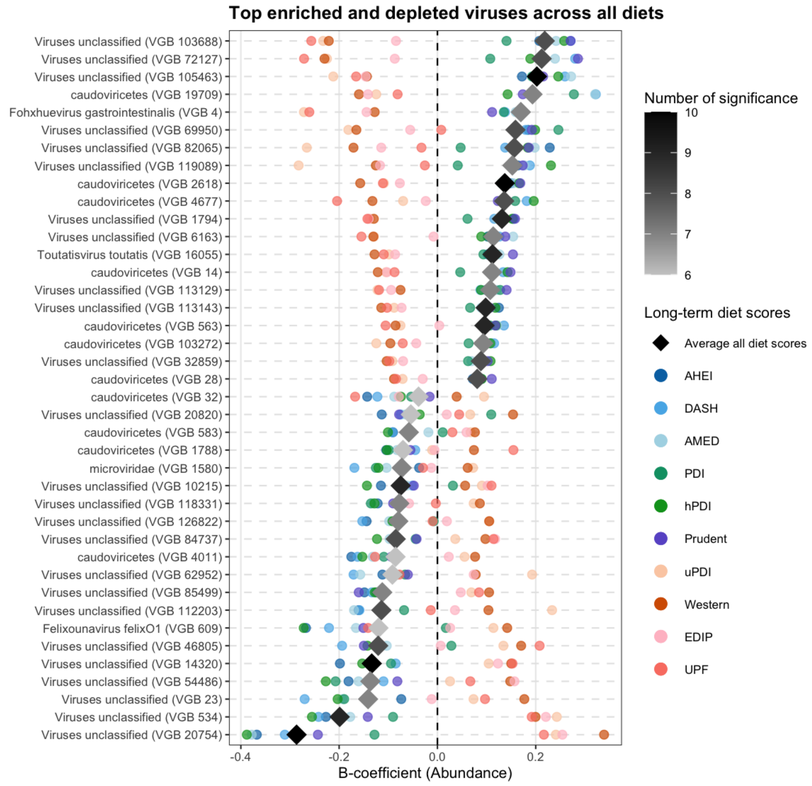

Figure 1. Top enriched and depleted viral taxa across long-term dietary patterns.
Colored circles represent regression β-coefficients for individual dietary scores. Black diamonds represent the average β-coefficient across dietary scores, with grey-scale color indicating the number of significant associations (q < 0.2). To align interpretation across dietary patterns, β-coefficients for unhealthy dietary scores were directionally flipped before calculating average β-coefficients.

- Several known bacteriophages were prioritized and significantly associated with long-term healthy diet, including *Fohxhuevirus gastrointestinalis* (enriched), *Toutatisvirus toutatis* (enriched) and *Felixounavirus felixO1* (depleted), as well as viruses in the class caudoviricetes (Beta-coefficient = 0.05–0.2, FDR < 0.2). **(Figure 1)** In contrast, associations for the top enriched and depleted viral taxa were generally reversed for unhealthy dietary patterns.
- We prioritized enriched and depleted bacterial taxa that significantly associated with long-term healthy diet.
- Among the top diet-associated taxa, iPHoP identified several high-confidence host–phage pairs (confidence score >90), including *Toutatisvirus toutatis–Faecalibacterium prausnitzii* with a positive abundance correlation (R = 0.6, p < 2.2×10^{-16}) and *Fohxhuevirus gastrointestinalis–Bacteroides eggerthii* with a negative abundance correlation (R = −0.21, p = 0.00016) **(Figure 2)**.

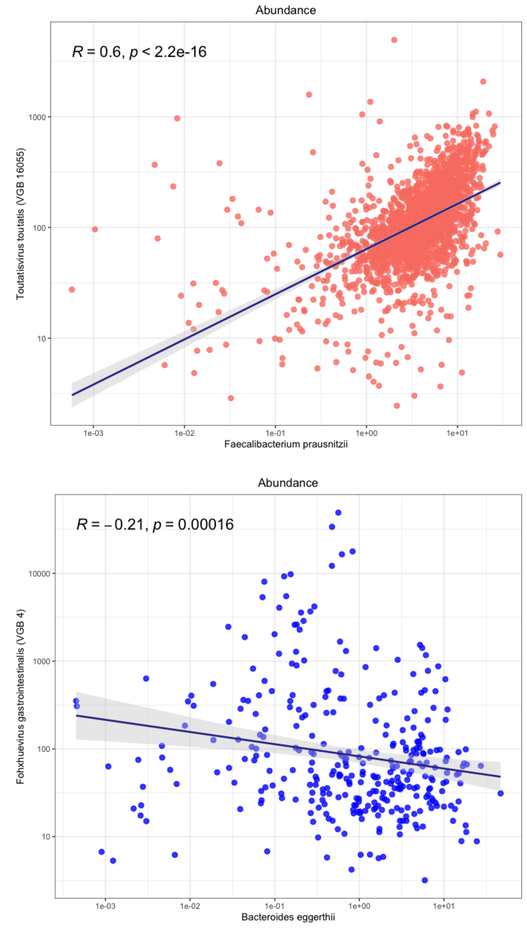

Figure 2. Correlations between predicted host–phage pairs.
Scatter plots showing abundance correlations between host–phage pairs.

CONCLUSION

Dietary patterns are associated with the gut virome in a taxon-specific manner. Associations with specific bacteriophages suggest that diet may influence gut *bacterial* structure through targeted ecological shifts.
Further studies are needed to clarify the effects of diet and the underlying phage–host dynamics.

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