Gut Microbiome and Virome Associated with Diabetes in Boston-Area Puerto Rican Adults

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BACKGROUND AND OBJECTIVE

Bacterial species associated with T2D in MaAsLin2 model[‡] adjusted for Metformin:

The gut microbiome has been implicated in the etiology of type 2 diabetes (T2D) and insulin sensitivity. Little work exists on relationships between gut bacteria, virome, and T2D in Puerto Ricans, who are at an increased T2D risk. To examine the relationships between the composition and function of the gut microbiome, gut virome and T2D in the Boston Puerto Rican Health Study.

METHODS

Data Source: 321 Boston Puerto Rican Health Study (BPRHS) participants with metagenomic profiling of stool samples

Statistical Analysis:

- Permutational multivariate analysis of variance (PERMANOVA) on Bray-Curtis dissimilarity was performed using R adonis2 function to test whether participants with T2D differ in β diversity of bacterial and viral composition compared to those without T2D.
- Feature-wise multivariable association analysis was performed using MaAsLin2 to identify associations between microbial species and viral genome bins (VGBs) and metadata variables.
- The q-value (FDR-adjusted p-value) for false positives was set to 0.25.

RESULTS

Community Ecology of microbiome and virome in T2D and key covariates (PERMANOVA):*

Covariate	R ² with BC matrix of bacteria	P-value	R ² with BC matrix of viruses	P-value
Diabetes (Yes)	0.00503	0.034	0.00339	0.374
MedDiet	0.00625	0.007	0.00480	0.045
Sex (Female)	0.01251	0.001	0.01125	0.003
Metformin use (Yes)	0.00810	0.099	0.00705	0.295
PPI use (Yes)	0.00557	0.011	0.00457	0.098
Physical Activity	0.00462	0.057	0.00520	0.025

Rest of covariates are not statistically significant for both bacterial and viral composition.

Metformin AN important confounder in microbiome-diabetes relationship:

Microbial species associated with diabetes from MaAsLin2 model[†] without adjustment for Metformin:

Species	Coefficient	FDR
Escherichia coli	2.26	0.04
Rothia mucilaginosa	1.12	0.11
Clostridiaceae bacterium	-1.03	0.16
Faecalibacterium prausnitzii	-1.48	0.17

Microbial species associated with diabetes from MaAsLin2 model[‡] with adjustment for Metformin:

Species	Coefficient	FDR
Collinsella aerofaciens	0.78	0.21
Alistipes sp AF17_16	-1.37	0.23
Acidaminococcus intestini	2.14	0.24

• †Covariates used in model 1: Mediterranean Diet (MedDiet), T2D status, age, sex, and BMI

- \$Model 2: Model 1 + Metformin use
- *Model 3: Model 2 + Bristol stool scale, fiber score, proton pump inhibitor use, laxative use, antibiotic use, physical activity score, alcohol use, and smoking status



Microbial Pathways associated with diabetes from MaAsLin2 model 2[‡] adjusted for Metformin

Pathways	Coefficient	FDR
superpathway of anaerobic sucrose degradation	0.28	0.16
TCA cycle IV (2-oxoglutarate decarboxylase)	1.21	0.22
L-glutamate degradation XI (reductive Stickland reaction)	1.14	0.22

Metformin AN important confounder in virome-diabetes relationship:

VGBs associated with diabetes from MaAsLin2 model 1[†] without adjustment for Metformin

VGBs Genus:Reference Species	Coefficient	FDR
Caudoviricetes: VGB_39162	-0.69	0.004
Casjensviridae: Felixounavirus felixO1	2.05	0.079
Peduoviridae: Lambdavirus lambda	1.85	0.081
Peduoviridae: Peduovirus P2	1.12	0.081
Caudoviricetes: VGB_103294	-1.93	0.130

No VGBs were significantly associated with T2D in MaAsLin2 Model[‡] after adjusting for Metformin use

CONCLUSION

- β diversity of bacterial species in participants with T2D is different versus those without T2D
- No statistically significant difference was observed in VGB β diversity between participants with T2D versus without T2D
- Several microbial taxa including *Collinsella aerofaciens, Alistipes sp. AF17-16* and *Acidaminococcus intestini* were associated with T2D
- Metformin is a strong confounder in microbiome/virome T2D relationship

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