Multi-omics Analysis of Oral Microbiome and Atherosclerosis in Women and Men with HIV

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BACKGROUND

Although alterations in gut microbiota have been implicated in both HIV and atherosclerotic cardiovascular disease, the role of the oral microbiota remains less understood, particularly regarding their potential connections to host immunity and inflammation in the context of HIV.

METHODS

- We examined associations of oral microbial features (measured by 16S rRNA sequencing) with carotid artery plaque (focal intima-media thickness >1.5 mm, assessed by B-mode carotid artery ultrasound) in 420 participants (265 women, 63% HIV+; 155 men, 54% HIV+) from the MACS/WIHS Combined Cohort Study.
- We measured 59 circulating proteomic inflammation markers by Olink platform.
- We further integrated plaque-associated oral microbial features with these proteomic inflammation markers.
- Multivariable logistic/linear regression models were performed, adjusting for demographic, behavioral factors, and HIV status. Benjamini-Hochberg FDR method was applied.

RESULTS

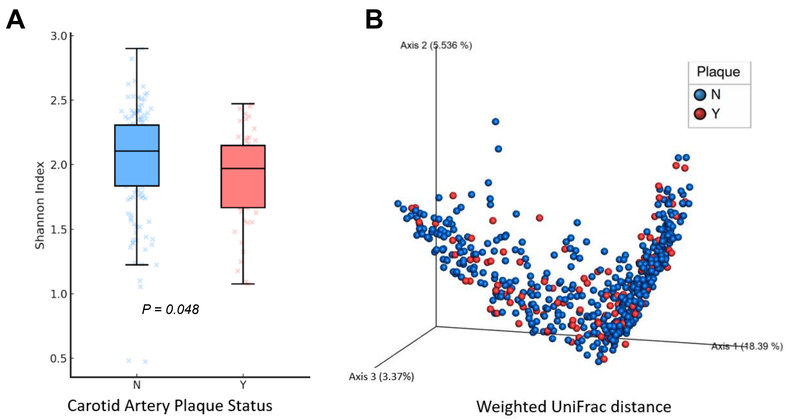
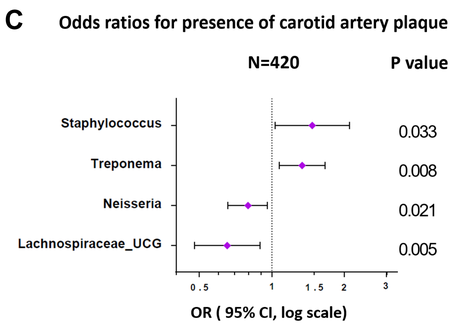


Figure 1. Microbial community-level and taxonomic analysis.

(A) α-diversity analyses (Shannon index) by carotid artery plaque status.

(B) Principal coordinates analysis (PCoA) of β-diversity using weighted UniFrac distances.
PERMANOVA R^2 =0.018, P>0.05, Permutation time =5000



(C) Associations between oral microbial taxa and carotid artery atherosclerosis. (multivariable logistic regression).
Results are odds ratios (ORs) and 95% confidence intervals (CIs) for carotid artery plaque per standard deviation increment of CLR transformed abundance of oral microbial genera, adjusted for age, race, sex, study site, antibiotics use, income, education, BMI, alcohol, smoking status, and HIV status.

- Results were consistent in women and men, and in those with and without HIV.

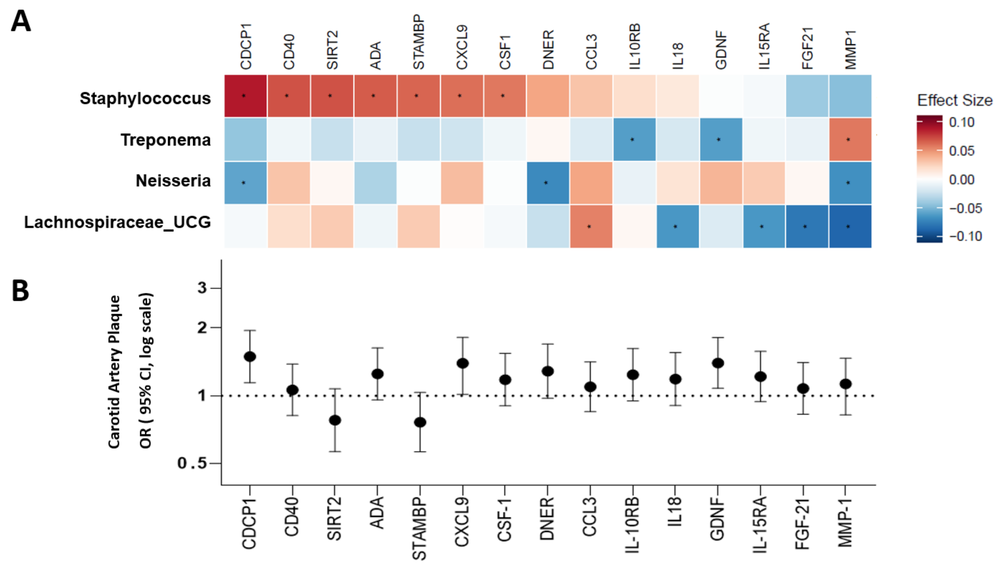


Figure 2 . Associations of Plaque-associated oral bacterial genera with host circulating proteomic inflammatory markers.
(A) Associations between plaque-associated genera and proteomic inflammatory markers.
Models were adjusted for age, race, sex, study site, antibiotics use, income, education, BMI, alcohol, smoking status, and HIV status. (* FDR P <0.05).
(B) Associations between these microbial associated proteomic inflammatory markers and carotid artery Plaque status . Models were adjusted for the aforementioned covariates.

- The oral microbial genera Neisseria and Lachnospiraceae were associated with lower odds of plaque, while Treponema and Staphylococcus were positively associated with plaque.

- These plaque-associated taxa were associated with 15 circulating inflammation markers. E.g., *Staphylococcus* (its DNA was detected in plaque samples), was associated with 7 inflammation markers, including CXCL9 (a pro-inflammatory chemokine associated with atherosclerosis risk), CD40 (reported with pro-inflammatory effects, higher CVD risk), ADA (a marker of vascular dysfunction), and CSF1 (a driver of macrophage-mediated inflammation).

- Associations between bacterial species and plaque were attenuated after further adjustment for specific microbial associated circulating metabolites and proteomic inflammatory markers.

CONCLUSIONS

We identified several oral bacterial taxa associated with carotid artery atherosclerosis, with certain microbiota-related inflammation markers partially explaining these associations. Our findings highlight potential oral microbiota–related targets for CVD prevention in people living with or at risk of HIV.