Changes in gut microbiota associated with progression of atherosclerosis in people with HIV

767

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BACKGROUND

Variations in gut microbiome might modulate host immune activation and inflammation, potentially linked to increased cardiovascular risk. Our objective was to longitudinally characterize the distinctive features of gut microbiota associated with progression of atherosclerosis measured through carotid artery intima-media thickness (cIMT) in people living with HIV (PWH).

METHODS

96-week, prospective longitudinal study in virologically-suppressed (HIV-1 RNA <50 copies/mL) PWH. cIMT was measured at baseline, 48 and 96-weeks visits using B-mode ultrasound at 6 locations. cIMT progression was defined as an increase >10% and/or detection of new carotid plaques. To profile the gut microbiome, DNA was extracted from fecal samples and quantified with the Qubit dsDNA HS Assay Kit. Amplification and sequencing of 16S ribosomal RNA (V3-V4 variable regions) were carried out following the Illumina protocol. The sequencing was performed with MiSeq platform.

RESULTS

202, 190 and 169 patients had available fecal samples for microbiome analysis at the baseline, 48- and 96-week visits, respectively. At the 96-week visit, 87 (43%) participants showed atherosclerosis progression, with 54 (26·7%) of them presenting a new carotid plaque. Clinical characteristics are shown in Table 1. The gut microbiota composition experienced low-sized significant intra-individual and interindividual changes during the study period. No significant differences were observed in α-diversity indices between groups defined by cIMT progression (Fig 1). Beta-diversity determined through principal coordinate analysis distances showed that the groups exhibited distinct microbial profiles (PERMANOVA p-value=0·03; Fig 2). Multivariate adjustment for traditional cardiovascular risk factors and body-mass index with an analysis of compositions of microbiomes with bias correction-2 (ANCOM-BC2) revealed that cIMT progression was consistently associated with Agathobacter and Ruminococcus_2 genera, while non-progression was consistently associated with Prevotella_7 (Fig 3).

Subclinical atherosclerosis progression and non-progression were consistently and independently **associated with a distinctive gut microbiota signature**

Table 1. Clinical characteristics of participants.

	cIMT progression		
	Yes	No	*p value*
Patients, no.	87 (45.5)	104 (54.5)	-
Male sex	71 (81.6)	82 (79.6)	0.854
Age, years	53 (46-58)	44 (35.8-51)	0.001
Cardiovascular risk factors, n (%)			
Current smoking	45 (51.7)	51 (49)	0.772
Hypertension	13 (14.9)	6 (5.8)	0.051
Dyslipidemia	17 (19.5)	5 (5)	0.003
Diabetes	3 (3.4)	2 (1.9)	0.662
Framingham risk score	11 (5.5-20.3)	4.8 (3.1-8.1)	0.001
ASCVD risk score	5.9 (2.4-11)	1.8 (1-3.7)	0.001
HIV-related factors			
CD4 T-cell count nadir, cells/µL	245 (139-318)	254 (147-411)	0.293
CD4 T-cell count, cells/µL	654 (450-876)	719 (544-866)	0.218
CD4/CD8 ratio	0.9 (0.7-1.3)	0.9 (0.7-1.3)	0.244

Figure 1. Adjusted gut microbiota α-diversity by Framingham risk score, CD4 T-cell count and baseline cIMT at the genus level by cIMT progression.

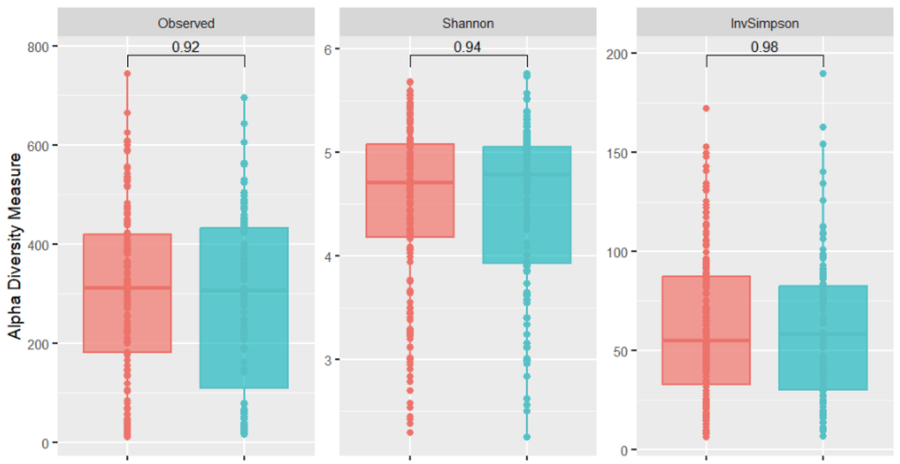


Figure 2. Gut microbiota beta-diversity through PCoA by cIMT progression.

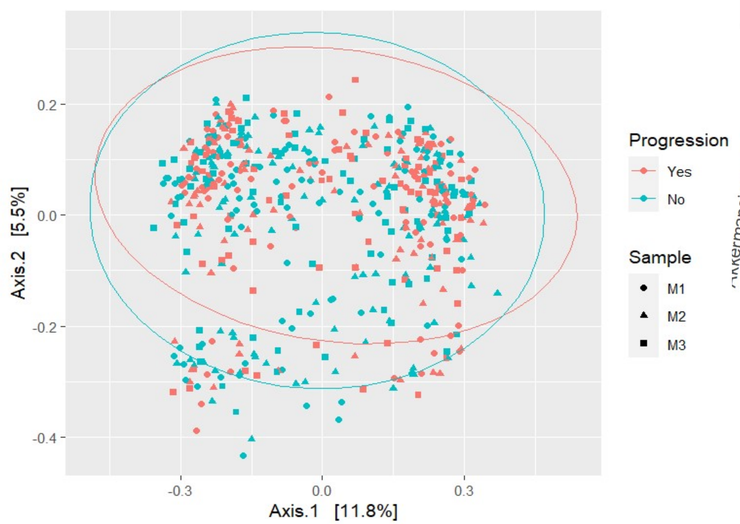
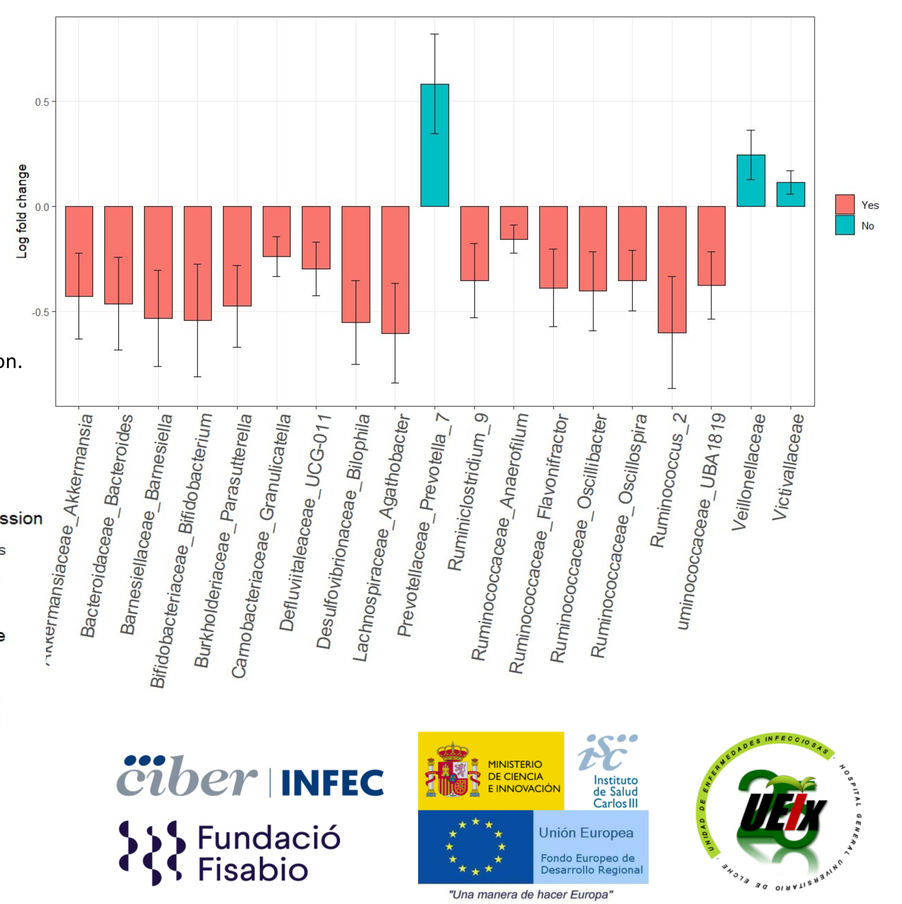


Figure 3. ANCOM-BC in relation to c IMT progression.



CONCLUSIONS

Progression of atherosclerosis in PWH is associated with distinctive signatures in the gut microbiota.

ADDITIONAL KEY INFORMATION

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Acknowledgements:

This work was supported by Spanish National Plan for Scientific and Technical Research and Innovation, European Regional Development Fund (ERDF) and Instituto de Salud Carlos III (ISCIII) (RD16/0025/0038, PI16/01740, PI18/01861, CM19/00160, CM20/00066, COV20/00005, CM21/00186, CM22/00026 and PI22/01949); CIBER, ISCIII, Ministerio de Ciencia e Innovación and European Union–NextGenerationEU (CB21/13/00011); Generalitat Valenciana (AICO/2021/205).

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