Activated and exhausted CD8+ T Cell subsets associate with carotid atherosclerotic plaques in PLHIV

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BACKGROUND

- Atherosclerotic cardiovascular disease (ASCVD) is one of the leading causes of morbidity and mortality in people living with HIV (PLHIV).
- Flow cytometry allows identification and quantification of immune cells within heterogenous populations.
- In this study we analysed associations between circulating immune cells and carotid plaque presence in PLHIV.

METHODS

Design:

Cross-sectional data from the 2000HIV cohort

Participants

PLHIV on long-term antiretroviral therapy (ART) without previous cardiovascular event (n = 1188), divided in discovery (n= 994) and validation (n= 194) cohort.

Instruments:

- Plaque: carotid artery 2-dimentional ultrasound. Definition: focal intima media thickness (IMT) ≥ 1.5mm or thickening of the IMT > 50% compared to the mean IMT in the common carotid artery, carotid bulb or internal carotid artery.
- High dimensional flow cytometry of whole blood to identify 403 cell populations.

Statistical analyses

- Absolute counts of cell populations were rank based transformed to meet normal distribution.
- Linear regression model adjusted for age, sex and seasonality.
- Findings in discovery cohort after correction for multiple testing (False discovery rate (FDR) < 0.05) were validated in validation cohort.

Activated and exhausted CD8+ T cell subpopulations are higher in PLHIV with carotid plaques

RESULTS

Table 1: Baseline characteristics

	Discovery cohort (n = 994)	Validation cohort (n = 194)
Age	51 [42-58]	52 [46-59]
Male sex	824 (83%)	161 (83%)
BMI	24.8 [22.3-27.6]	25.6 [22.4-28.4]
Current smoking	294 (30%)	52 (27%)
Hypertension	195 (20%)	47 (24%)
Lipid lowering drug	121 (12%)	35 (18%)
Carotid plaque	502 (51%)	82 (42%)
CD4 nadir	260 [140-400]	260 [120-370]
Most recent CD4	700 [540-900]	660 [460-810]
HIV duration, years	12.8 [7.5-19.3]	11.0 [5.9-18.1]
cART duration, years	10.4 [6.2-16.3]	9.2 [5.0 – 15.3]

Figure 1: Correlation plot carotid plaque presence with immune cell subsets; discovery and validation cohort

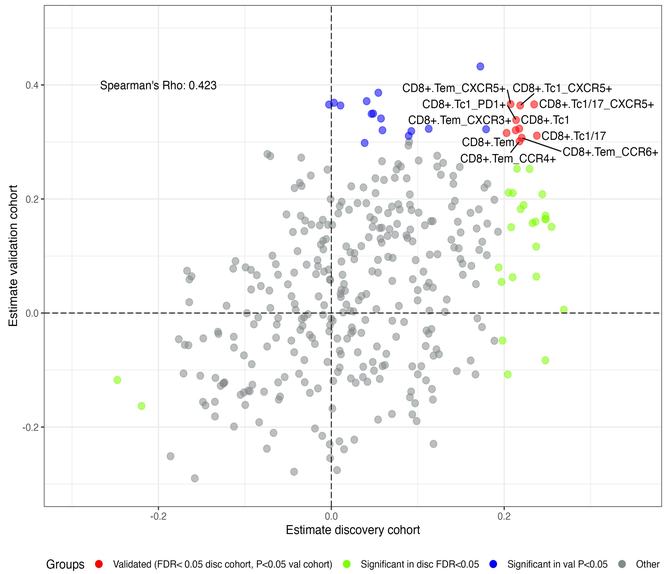
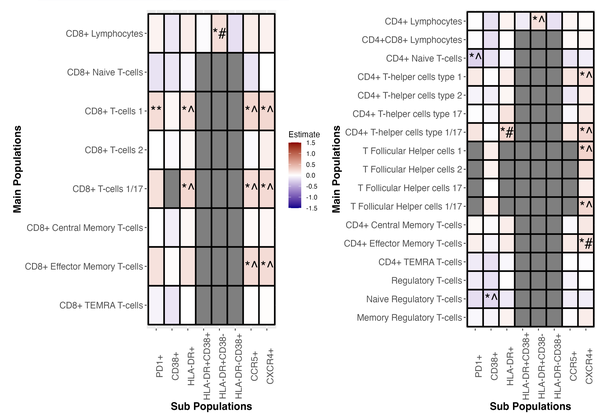


Figure 2: Heatmap absolute counts CD8 and CD4 T cells main and subpopulations



Estimate of discovery cohort is shown.

** indicates significant difference between participants with and without carotid plaques in both discovery (FDR < 0.05) and validation cohort (P < 0.05)

*^ indicates significance in the discovery cohort (FDR < 0.05) and equal directionality change of the estimate in the validation cohort without significance

*# indicates significance in the discovery cohort (FDR < 0.05) but with opposite change in the validation cohort without significance.

CONCLUSIONS

- Levels of circulating CD8+ T cell populations were significantly higher in PLHIV with carotid plaques compared to those without plaques.
- These alterations span activated (HLA-DR) and exhausted (PD1) cell phenotypes.
- Our findings underscore a potential role of CD8+ T cells in atherogenesis.
- Concurrent elevation of cytotoxic CD8+ T cells 1 ($CD8_{TC1}$) and $CD8_{TC1}$ expressing exhaustion marker PD1 provides further insight into the possible dynamic interplay of immune responses in atherosclerosis.

ADDITIONAL KEY INFORMATION

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www.2000HIV.com