ALDH Activity as a New Marker of Subclinical Atherosclerosis during ART-Treated HIV-1 Infection

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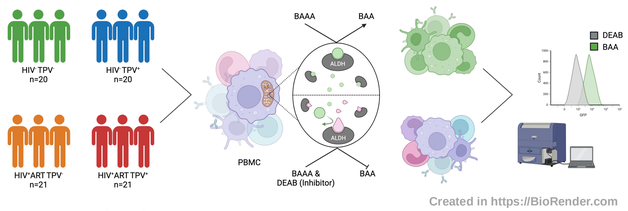
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BACKGROUND

Antiretroviral therapy **(ART)** controls viral replication in people with HIV **(PWH)**, but viral reservoirs **(VR)** persist and represent a cause for the occurrence of age-related comorbidities, e.g., cardiovascular disease **(CVD)**. We previously demonstrated that retinoic acid **(RA, a vitamin A derivative)** increases HIV-1 outgrowth from VR and that microbiota components **(*e.g.,* Staphylococcus aureus)** promote ALDH **(aldehyde dehydrogenase that converts vitamin A into RA)** activity in myeloid cells. We **hypothesized** that ALDH activity is a novel functional marker of immune activation that predicts subclinical atherosclerosis in ART-treated PWH.

METHODS

The study was conducted on PBMCs of ART-treated PWH **(HIV+ART; n=42)** and uninfected study participants **(HIV-; n=40)** from the Canadian HIV and Aging cohort Study **(CHACS)**, with/without subclinical coronary artery atherosclerosis visualized as total **(TPV)** and low attenuated plaque volume **(LAPV)**, and coronary artery calcium **(CAC)** score by computed tomography angiography. Flow cytometry was used for ALDH activity monitoring on immune cells identified based on the expression of lineage markers as dendritic cells **(DC, CD3$^-$HLA-DR$^+$CD1c$^+$)**, monocytes **(CD3$^-$HLA-DR$^+$CD1c$^-$)** subdivided in classical **(CD14$^+$CD16$^-$)**, intermediate **(CD14$^+$CD16$^+$)**, and non-classical **(CD14$^-$CD16$^+$)** monocytes and CD4$^+$/CD8$^+$ CD3$^+$ T cells.



Experimental Design

CONCLUSIONS

HIV-1 infection is associated with an increased frequency of ALDH+ myeloid and lymphoid cells, supporting use of ALDH activity as new functional marker for immune activation monitoring, independent of subclinical atherosclerosis and downregulated by statin treatment.

- **Overt ALDH activity** in monocytes of ART-treated PWH is associated with **calcified atherosclerotic plaque**
- **ALDH activity** is significantly reduced by **statin treatment**

RESULTS

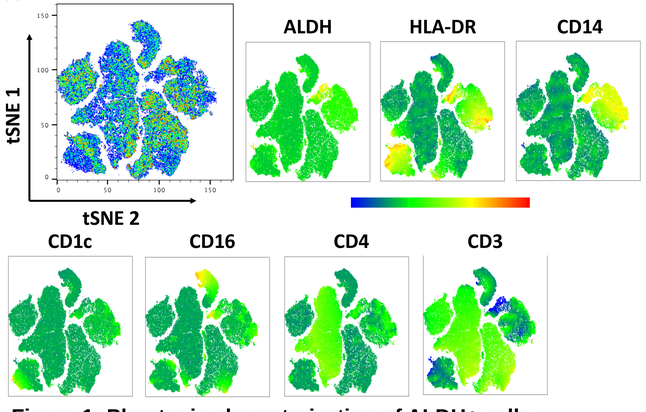


Figure 1: Pheptypic characterization of ALDH+ cells

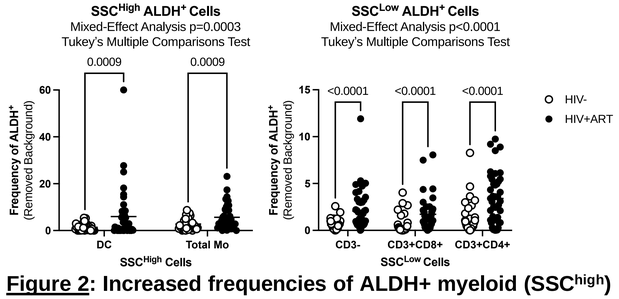


Figure 2: Increased frequencies of ALDH+ myeloid (SSC^{high}) and lymphoid (SSC^{low}) cells in HIV+ART *vs.* HIV- individuals

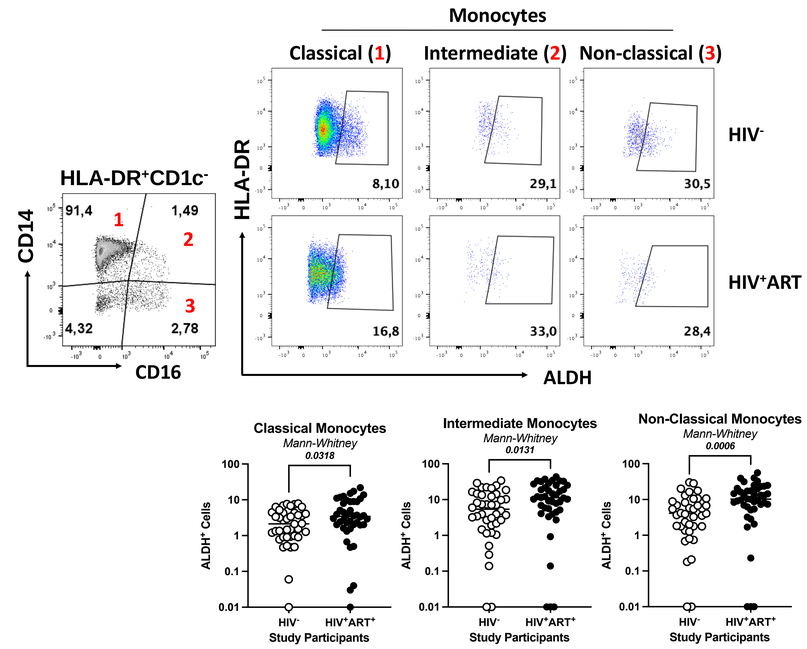


Figure 3: ALDH activity in monocyte subsets is increased in HIV$^+$ART *vs.* HIV$^-$

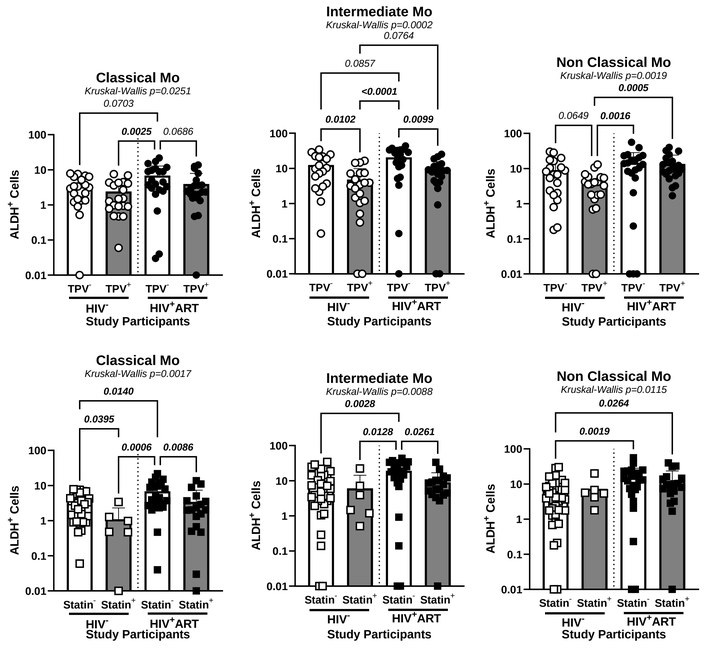


Figure 4: Reduced frequency of ALDH+ monocyte subsets in TPV$^+$ *vs.* TPV- HIV$^+$ART and HIV$^-$ individuals, likely as a consequence of statin treatment

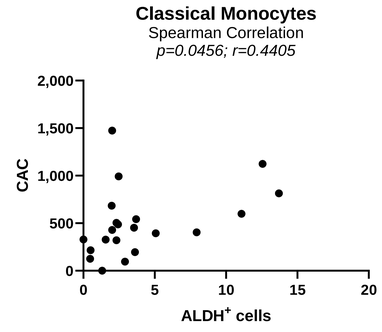


Figure 5: ALDH activity in classical monocyes positivelly correlates with calcified atherosclerotic plaque (CAC)

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