Longitudinal Phenotypic and Transcriptional Profiling of Immune Cells in Early-Treated Acute HIV

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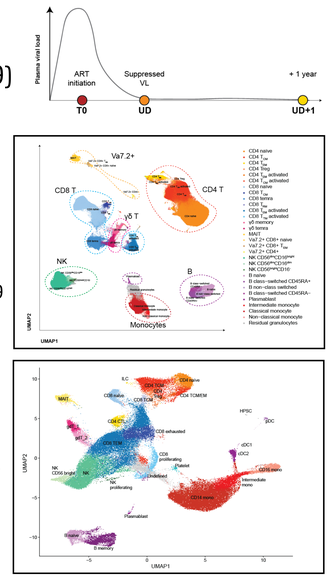
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BACKGROUND

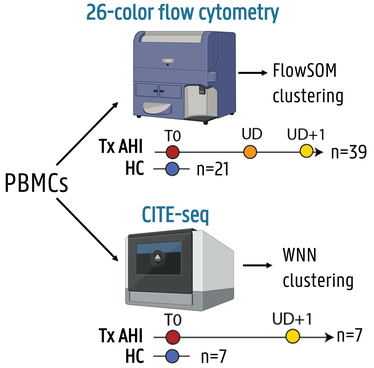
Despite early antiretroviral treatment (ART) initiation, **persistent immunological alterations** have been described in people living with HIV (PLWH) treated during **acute HIV infection** (AHI).

METHODS

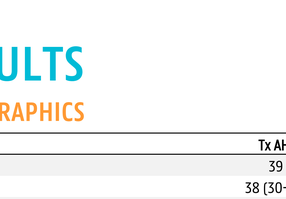
- Belgian **ACS study**
- Tx AHI= early treated cohort (n=39)
- HC= HIV- cohort (n=21)



26-color flow cytometry



CITE-seq



RESULTS

DEMOGRAPHICS

		Tx AHI	HC
n		39	21
Age		38 (30-44)	36 (33-45)
Sex			
	Male	33	13
	Female	3	8
CD4 nadir		428 (326-595)	/
CD4/CD8 nadir		0.52 (0.36-0.86)	/
Peak VL (log10 copies/mL)		6.51 (5.67-7)	/
Fiebig stage at treatment initiation			
	Fiebig II	8 (20.51%)	/
	Fiebig III	7 (17.95%)	/
	Fiebig IV	2 (5.13%)	/
	Fiebig V	20 (51.28%)	/
	Fiebig VI	2 (5.13%)	/

CD8 T CELLS REMAIN ELEVATED AND MONOCYTES DECREASE DESPITE EARLY ART

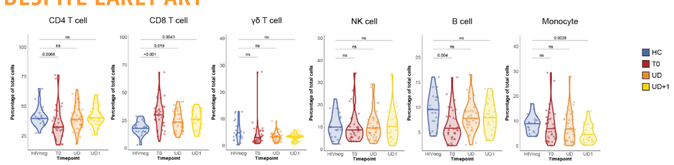


Figure 1 Violin plots displaying the relative abundance of CD4 T cells, CD8 T cells, γδ T cells, NK cells, monocytes and B cells longitudinally in Tx AHI, compared to HCs.

ART initiation during acute HIV infection (AHI) cannot fully prevent phenotypic and transcriptional changes in PBMCs.

VERY EARLY ART CANNOT PREVENT DISTINCT PHENOTYPICAL ALTERATIONS IN PBMCS

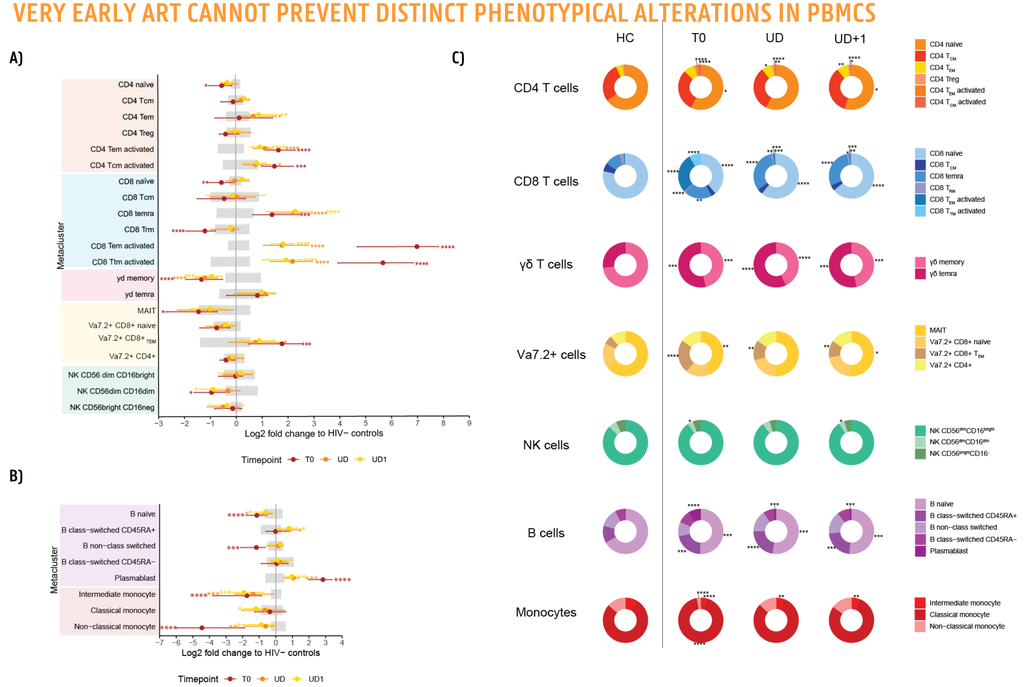


Figure 2 Bar chart representing median and interquartile ranges of normalized T and NK cell **(A)** and B cell and monocyte **(B)** metacluster proportions (% of total cells) in Tx AHI at T0 (red), UD (orange) and UD+1 (yellow) versus the median of HC (Log2 fold change). **(C)** Donut chart representing metacluster proportions within all PBMC compartments in Tx AHI at T0, UD and UD+1 versus HCs.

TERMINAL DIFFERENTIATION AND RESIDUAL ACTIVATION DEFINE PLWH TREATED DURING AHI

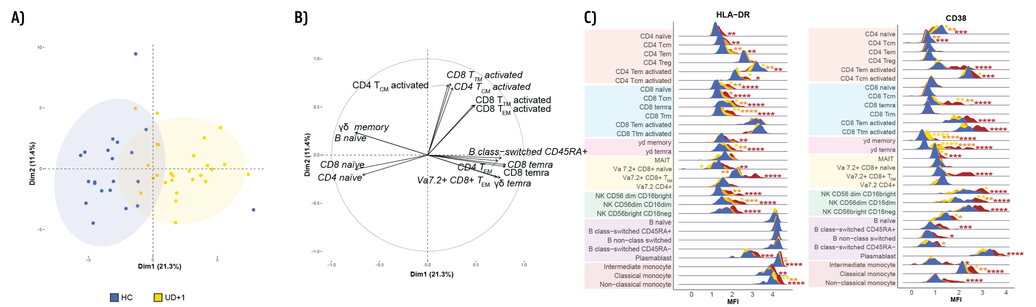


Figure 3 **(A)** Principal component analysis of the relative and proportional abundances of all metaclusters in Tx AHI at UD+1 (yellow) and HCs (blue). **(B)** Top 15 contributing factors to differentiate Tx AHI at UD+1 from HCs. Proportional abundances are italicized. **(C)** Ridgeline plot depicting MFI of HLA-DR and CD38 in Tx AHI at T0 (red), UD (orange) and UD+1 (yellow) and HCs (blue).

CITE-SEQ CONFIRMS DIFFERENTIALLY ABUNDANT CELLULAR CLUSTERS IN INDIVIDUALS TREATED DURING AHI

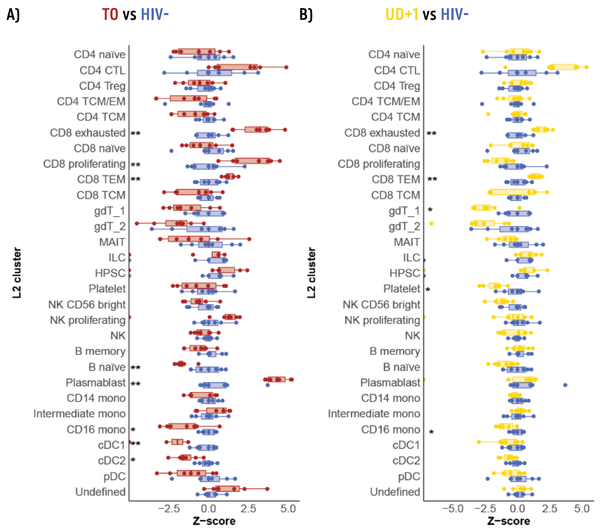


Figure 4 Stacked dot/box plots representing the abundance of each CITEseq metacluster (% of total cells) at T0 **(A)** and UD+1 **(B)**, normalized versus the median of HC (Log2 fold change).

CONCLUSIONS

- Early treated PLWH persistently show increased CD8 T cell and decreased monocyte proportions during viral suppression.
- Despite early ART, activated T cell metaclusters and TEMRA CD8 and γδ T cells are relatively enriched in PLWH.
- In monocytes, especially intermediate and non-classical monocytes are decreased during AHI and do not fully normalize with suppressive ART.
- Principal component analysis demonstrates that terminal differentiation of T cells and residual immune activation define individuals treated during AHI compared to HCs.
- CITE-seq confirms the expansion of CD8 T cells with an exhausted and effector memory profile and persistent decrease in non-classical monocytes during viral suppression.
- Further exploration of differential gene expression across subsets will reveal more insights into immune dysfunction in PLWH.

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