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EXPANDED CYTOTOXIC T-LYMPHOCYTES AND NK CELL SUBSETS IN INFANTS WITH PERINATAL HIV

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Background

In perinatal HIV infection, early ART initiation is recommended but questions remain regarding infant immune responses to HIV as well as the impact of HIV on early immune development. The adaptive immune system is immature in newborns and rapidly develops with exposure to pathogenic and environmental antigens. **The objective of the current study was to evaluate the immune cell landscape in response to perinatally acquired HIV infection in 1 month old infants.**

Methods

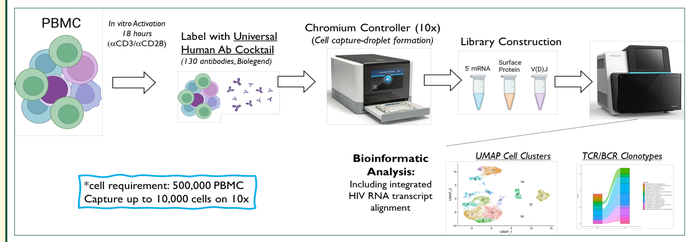
We investigated HIV-exposed infected (HEI, n=4) and HIV-exposed uninfected (HEU, n=3) 1-2 month old infants from the TARA (Towards AIDS Remission Approaches) Cohort from Maputo, Mozambique prior to ART-initiation..

Study Population

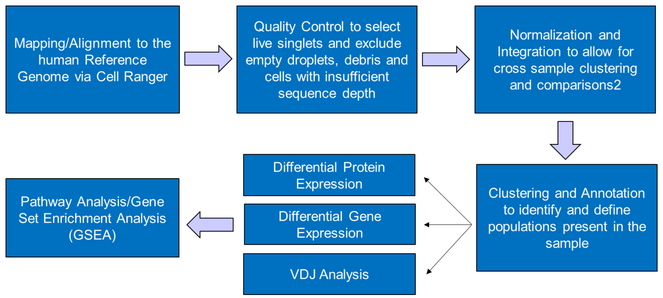
PID	Status	Time Point	Viral Load
CP002	HEI	1 month	$4x10^6$
CP003	HEI	1 month	$6x10^6$
CP006	HEI	1 month	$1x10^7$
CP018	HEI	1 month	$2x10^5$

PID	Status	Time Point
CE021	HEU	1 month
CE025	HEU	1 month
CE037	HEU	1 month

Multi-omic 10x scRNA-seq Workflow: Multi-omic sequencing and analysis was performed in cryopreserved PBMC



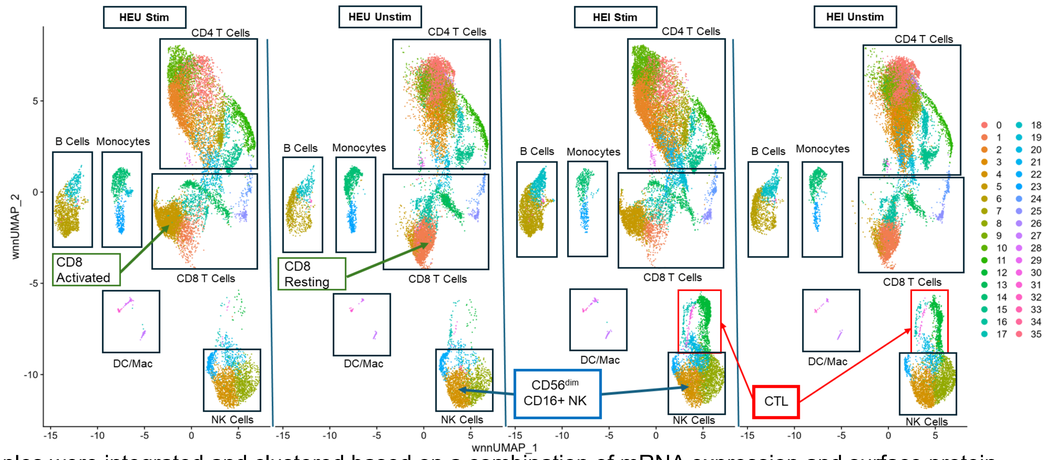
Bioinformatic Analysis Pipeline



Multi-omic single cell analysis reveals altered immune cell landscape in perinatal HIV infection. Cytotoxic T-Lymphocytes uniquely expanded in HEI show terminal effector phenotype (CD57+CD28-). CD56^{dim}CD16+ NK cells showed 388 differentially expressed genes in HEI related to leukocyte activation, T-cell regulation and immune effector processes

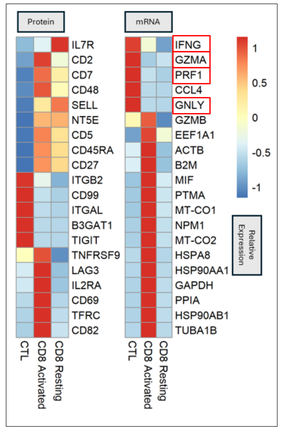
Results

I. Integration and clustering reveal CTL-like population in HEI which is absent in HEU

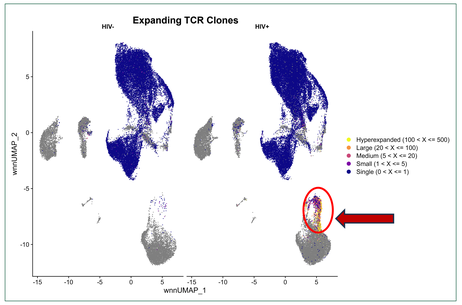


Samples were integrated and clustered based on a combination of mRNA expression and surface protein expression. The conditions are; HEU Stimulated (HEU with αCD3/αCD28 stimulation), HEU Unstimulated, HEI Stimulated (HEI with αCD3/αCD28 stimulation) and HEI Unstimulated. CD8+ Cytotoxic T-Lymphocytes (CTLs) were identified based on gene expression of cytotoxic molecules Granzymes, Perforin, Interferon Gamma and Granulysin.

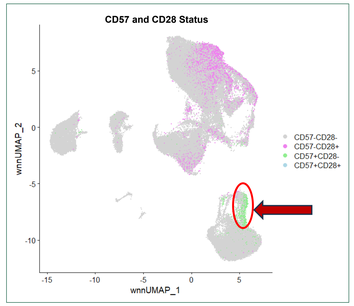
II. CTL-like cluster defined by expression of cytotoxic molecules



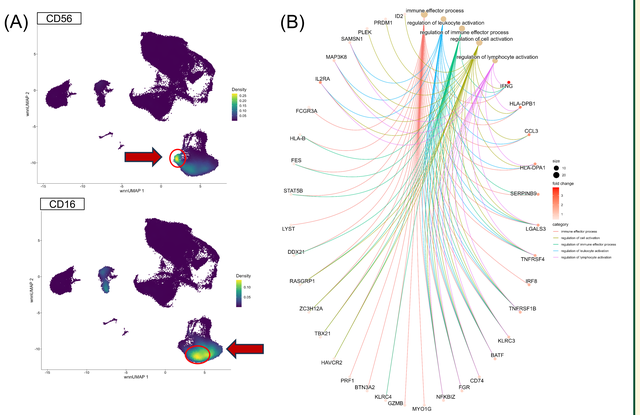
III. V(D)J analysis reveals CTL-like cluster made up of expanded clones



IV. CTL-like cluster are terminal effector phenotype (CD57+CD28-)



V. CD56^{dim}CD16+ NK in HEI exhibit enriched immune effector pathways



A. Feature Plot of CD56 and CD16 define NK populations.
B. Gene Set Enrichment of CD56^{dim}CD16+ NK Cells; showed activation of several inflammatory and immune effector pathways in HEI with a total of 388 differentially expressed genes. Most highly enriched pathways were related to leukocyte/ lymphocyte activation and T-cell regulation.

Conclusions

- Annotation and clustering of PBMCs from HEI and HEU shows an expansion of a unique CTL-like cluster in HEI
- V(D)J analysis reveals clonal hyperexpansion in the HEI infants but not in HEU
- CTLs were phenotyped using Antibody Derived Tags into CD57+CD28- and CD57-CD28-, with the majority of the CD57+ appearing on hyperexpanded clonotypes rather than monoclonal ones.
- CD56^{dim}CD16+NK cells show upregulation of immune effector pathways and cytotoxic pathways and T-cell regulation in HEI but not in HEU. They cluster similarly to the CTL-like population.
- The role of CTL and NK cells in virus control in infants with HIV is under investigation. See also poster 455

Acknowledgements

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