LONGITUDINAL T CELL IMMUNE PROFILING IN HIV EXPOSED INFECTED AND UNINFECTED INFANTS

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BACKGROUND

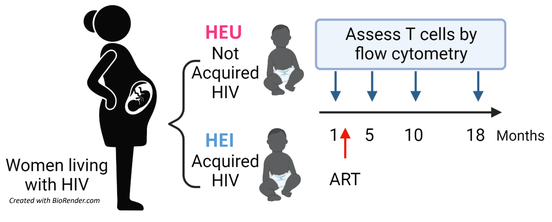
In perinatal HIV infection, early ART initiation is recommended but questions remain regarding infant immune responses to HIV as well as the impact of HIV on early immune development. The adaptive immune system is immature in newborns and rapidly develops with exposure to pathogenic and environmental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

METHODS

Towards AIDS Remission Approaches (TARA) Cohort from Maputo, Mozambique

	HIV-exposed Infected (HEI)	HIV-exposed Uninfected (HEU)
N, enrolled	43	**47**
Left study/Lost to follow-up	3	9
Died	4	2
Sero-converted	0	1
N, completed follow-up	36	35
Gender (M/F)	14/22	18/17
Age at Entry (wks)	5.7 (4.3-10.4)	5.7 (4.3-9.6)
VL log at Entry, median + SD	5.7+/-1.2	N/A
CD4 c/mm3 at Entry, median + SD	2211+/-909	N/A
Feeding Practice Maternal/Formula/Combo	29/2/4	28/1/5

- All infants were prescribed nevirapine at birth for 6 weeks. Upon positive HIV PCR test at 1-2 months of age, infants were prescribed AZT+3TC+lopinavir/ritonavir.
- 6/36 HEI exhibited sustained viral suppression during 2 year follow-up. Low viral suppression is attributed to lack of ART adherence in the cohort.

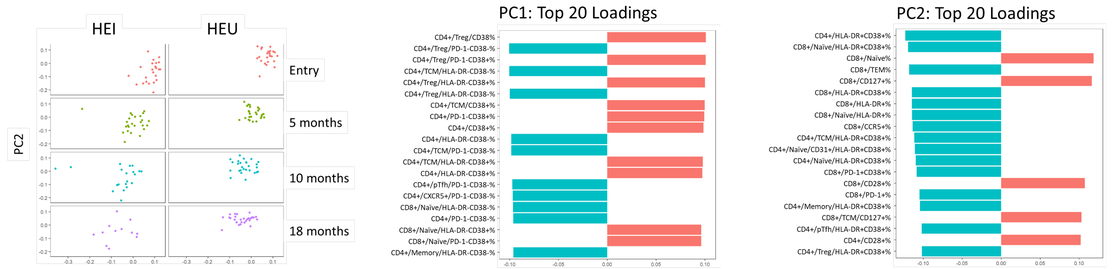


Samples for analysis	HEU	HEI
Entry (1-2 month)	35	33
5 month	33	28
10 month	30	27
18 month	31	15

Perinatal HIV infection alters some but not all features of T cell development in infants; CD8+ T cell expression of immune activation markers strongly correlates with plasma virus load at all ages with *increased expression of HLA-DR, PD-1 and CCR5* and *decreased expression of CD127* in comparison to age-matched, HEU infants.

RESULTS

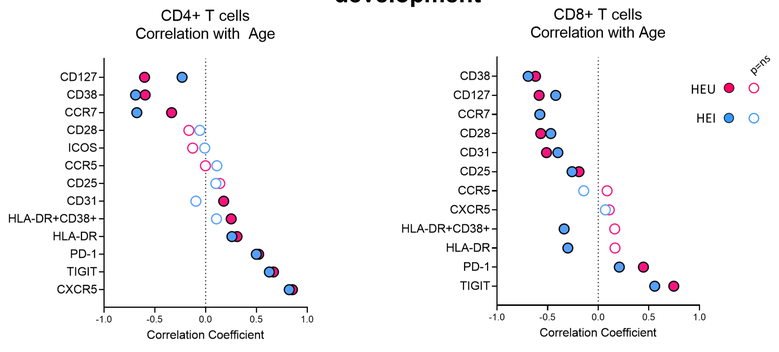
I. Different T cell variables associate with Age and HIV status in Longitudinal Analysis of Infants



- 382 T cell variables from longitudinal timepoints in HEI and HEU were assessed using Principal Component Analysis (PCA).
- Variation along PC1 was related to age in HEI and HEU while variation along PC2 differentiated between HEI and HEU at all timepoints.

***Non-linear Partial Least Squares (NIPALS) Algorithm was used to scale and center data (nipals package in R Wright, K; 2021).*

II. Multiple Surface Markers on T cells are closely associated with Age during Infant immune development

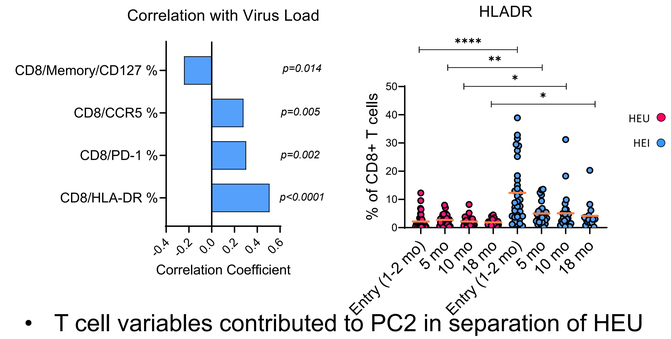


- In CD4+ T cells, expression of CXCR5, TIGIT, PD-1, HLA-DR and CD38 correlate with age and show no difference between HEI and HEU. Age-related changes in CD127, CCR7, and CD31 are altered in HEI.
- In CD8+ T cells, expression of CD38, CCR7, CD28, CD31, and CD25 correlate with age similarly in HEI and HEU. Age-related changes in PD-1, TIGIT, HLA-DR, and CD127 are altered in HEI.

***Spearman correlations were performed between age (months) and frequency data.*

RESULTS

III. T cell variables Associated with Virus Load in HEI



- T cell variables contributed to PC2 in separation of HEU and HEI *and* correlated with plasma virus load.
- HLA-DR+ CD8 T cells showed strongest correlation with virus load.
- HLA-DR and PD-1 were higher in HEI than HEU at all timepoints. CCR5 was higher at Entry and 18 months. CD127 was lower in HEI compared to HEU at all timepoints.

*** Spearman correlations were performed between VL and frequency data. Student's t test was used to determine differences between HEI and HEU.*

CONCLUSIONS

- The T cell compartment is highly dynamic in first 18 months of life in HEU and HEI.
- Perinatal HIV infection alters longitudinal expression of various surface receptors on CD4+ and CD8+ T cells.
- CD38 expression on both CD4+ and CD8+ T cells is a strong correlate of age and is not perturbed during HIV infection.
- CD4+ T cell variables were not associated with virus load in HEI despite being cellular target of HIV infection.
- Direct association of CD8+ T cell immune activation and virus load is also observed in Adult HIV infection suggesting infants are responding similarly despite an immature and tolerogenic immune environment.

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