PEA0024

Aging B-cells (ABC) and anti-Env humoral responses are associated with T-bet expression in B-cells of perinatally HIV infected children (PHIV) treated within 24 months of life (the CARMA cohort)

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BACKGROUND

The role of T-bet, an immune factor involved in adaptative and innate response, has been poorly explored in B-cells. Previous studies concentrated on HIV+ and HIV- adults, but not children, and T-bet was found to be associated with ABC.

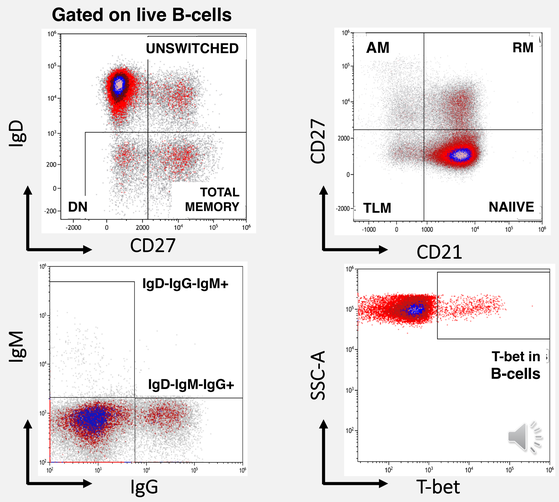
AIM

To characterize T-bet expression in Aging B-cell (ABC) subsets including Activated Memory (AM, CD21-CD27+) and Double Negative (DN CD27-IgD-), alongside the anti-HIV response analysed with IgG+ B cells in PHIV.

METHODS

We studied 40 PHIV starting antiretroviral (ART) at median 4.1 months of age and ART-suppressed for >5 years alongside 20 age and gender-matched controls (HC). B-cell phenotype and intracellular T-bet (MFI) was measured by Flow Cytometry. Anti-HIV serology was measured using Western blot and ELISA. Intracellular HIV-1 DNA using digital droplet PCR. Comparisons were analysed using Mann-Whitney test (MW). Associations were explored using Spearman test (rho, p) and multivariable ridge Poisson Regression model including baseline CD4, gender, and age at ART as confounders.

GATING STRATEGY



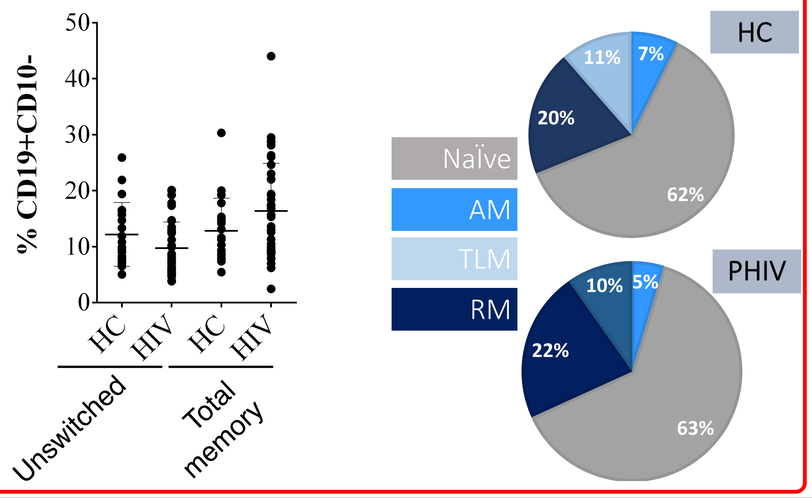
STUDY POPULATION

	PHIV (N=40)	HC (N=20)	p
Gender F, N (%)	27/40(68%)	13/20 (65%)	1.0[a]
Age, median years (IQR)	12.9 (8.7-16.6)	11.3 (7.6-16.1)	0.42[b]
Age at ART start, median months (IQR)	4.1 (0.3-6.2)	na	na
Time on ART, median years (IQR)	13.5 (8.1, 16.5)	na	na
Total HIV-1 DNA, median copies/10^6 PBMC (IQR)	48.4 (7.0-112.4)	na	na
Anti-HIV WB Env[c] positive, N (%)	10/38 (26%)	na	na
Anti-HIV ELISA gp41 median µg/ml (IQR)	2.6 (0.8-5.3)	na	na
Anti-HIV ELISA gp160 median µg/ml (IQR)	7.6 (1.8-15.2)	na	na

[a] Chi-square (F exact test); [b] t-test; [c]ENV= gp41, gp120, gp160

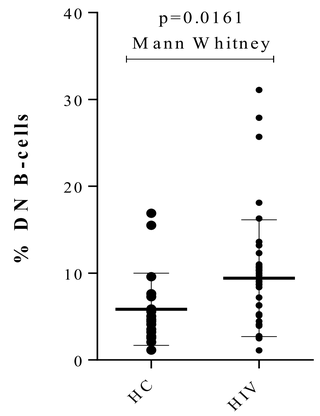
RESULT I

B cells phenotype is comparable between HC and PHIV



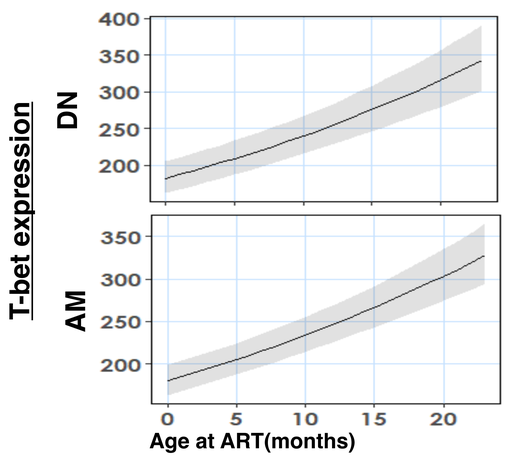
RESULT II

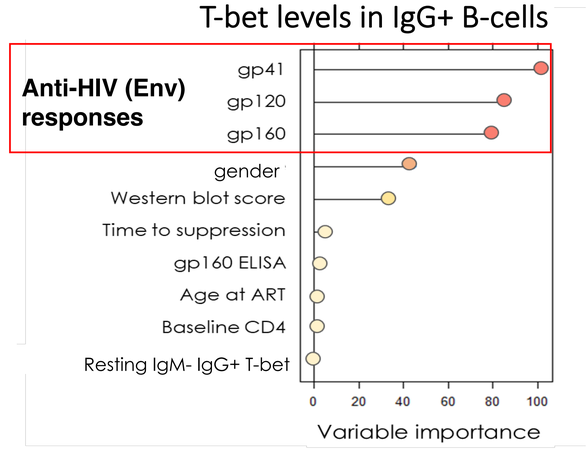
DN were expanded in PHIV compared with HC (p=0.01 MW)



RESULT III

T-bet expression is not associated with viral correlates. Time of ART start is associated with T-bet levels: for each month without ART T-bet increased by 3% and 2% in DN and AM, respectively (left panel). Anti-HIV (Env) responses were identified as predictors of T-bet levels in switched IgD-IgM-IgG+ B-cells (rho=0.35, p=0.03), IgD-IgG-IgM+ B-cells (rho=0.39, p=0.01), and RM IgM+ (rho=0.33, p=0.042).





CONCLUSIONS

ABC subsets are expanded in PHIV compared with HC and later ART-start corroborates the expansion of ABC, confirming the importance of early ART-start for preservation of B-cells functionality. The role of T-bet in the anti-HIV-specific B-cells response warrants further studies.

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