Severe depletion and exhaustion of mucosal-associated invariant T (MAIT) cells in HIV-1 infected patients

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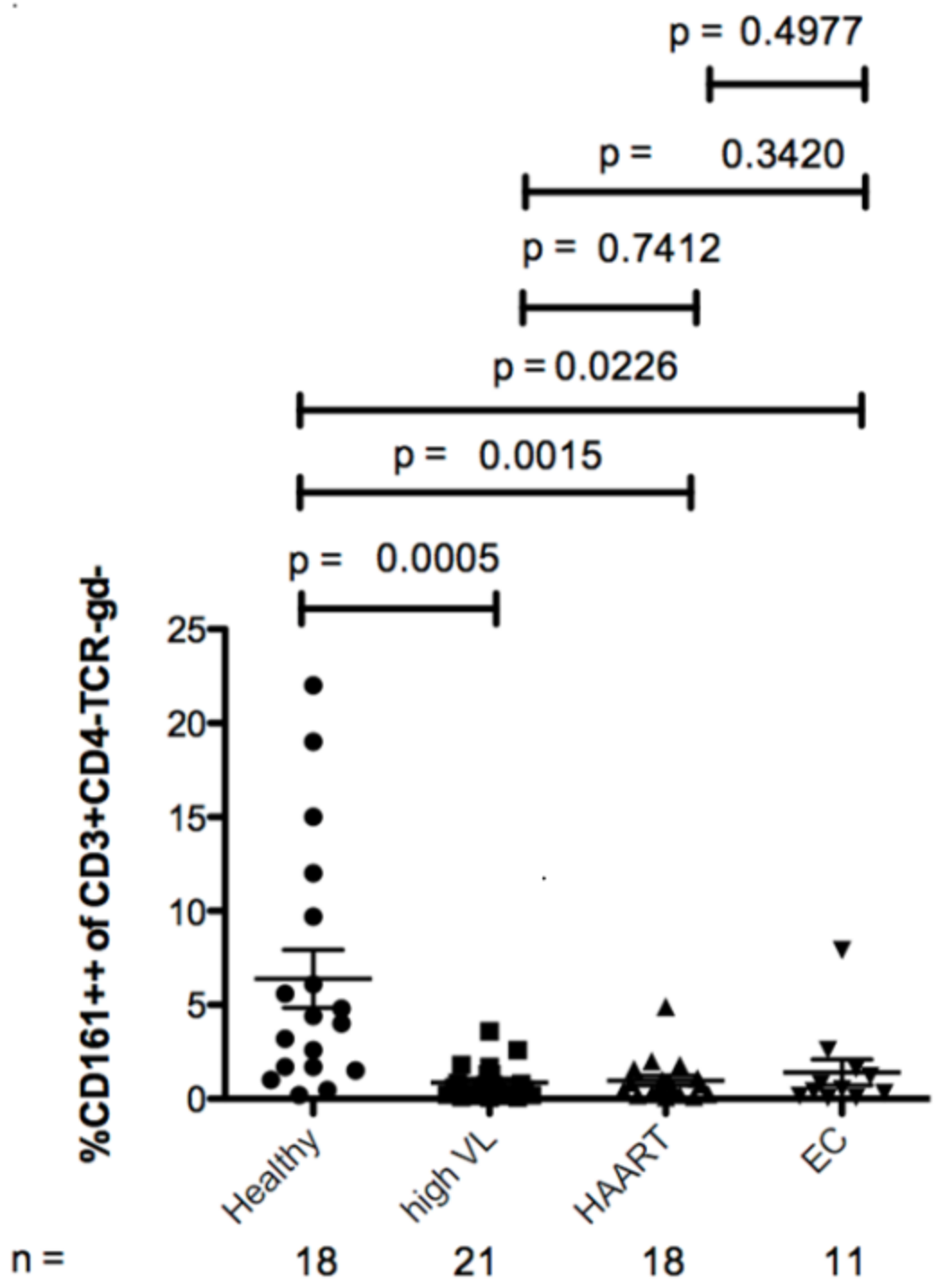
Background: Mucosal-associated invariant T (MAIT) cells compromise an evolutionarily conserved class of T-cells that act as a bridge between innate and adaptive immunity. They are characterized by the expression of the semi-invariant TCR Vα7.2 that recognizes antigens presented by MHC class I related (MR1) protein. Their ability to be stimulated by bacterial-metabolism derived B-vitamin-derivatives suggests a role in host defence against bacterial pathogens.

Methods: We studied the frequency and distribution of MAIT cells defined as CD3+CD4-TCRγδ-CD161++ lymphocytes in different groups of HIV patients and healthy controls.

Results: We show that MAIT cells are drastically depleted from the peripheral blood of HIV-infected patients. Their frequency is reduced from 6.38% (mean frequency of CD3+CD4-TCRγδ- lymphocytes) in healthy individuals to 0.87 % in HIV infected patients with a viral load of >100.000 copies/ml ($p < 0.0005$). They are not reconstituted in patients receiving antiretroviral treatment (0.98%) and only slightly less depleted in elite controllers (1.41%). Moreover, residual MAIT cells in HIV-progressors show a significantly elevated expression level of the exhaustion marker PD-1 (34.62% of MAIT cells are PD-1+ in HIV patients with VL>100.000 compared to 23.17% in healthy donors, $p=0.018$). MAIT cells from elite controllers show a nonexhausted phenotype (25.13%) and the exhaustion is partially reversed in HAART treated patients (28.61%).

Conclusion: The loss and exhaustion of MAIT cells could have important implications for the mucosal defence against bacterial pathogens, particularly in the gut of HIV-infected patients.


p = 0.4977
p = 0.3420
p = 0.7412
p = 0.0226
p = 0.0015
p = 0.0005
%CD161++ of CD3+CD4-TCR-gd-
25
20
15
10
5
0
Healthy
high VL
HAART
EC
n =
18
21
18
11

[Graph 2]