

INTRODUCTION

Background
 CD160 is a glycosylphosphatidylinositol (GPI)-anchored protein member of the Ig-superfamily and expressed on T cells and NK cells. Engagement of CD160 on activated CD4+ cells provides negative signals to CD4+ lymphocytes and inhibits proliferation. However its function and expression on HIV-specific CD8+ T cells is less clear.

Objectives
 The interplay between costimulators (CD28,LIGHT) and attenuators (BTLA,PD-1) ultimately determines the downstream functions of responding lymphocytes. Therefore our study aims to characterize the expression levels of CD160 on HIV and CMV specific cells during different stages of HIV disease and measure simultaneously its expression with markers of T cell exhaustion such as PD-1.

Methods
 We analyzed the relative expression of PD-1 and CD160 on HIV and CMV-specific cells from 44 HIV-infected individuals and 9 seronegative controls. We subdivided the population into 5 groups: Acute infection (n = 12; infected for less than 6 months, chronic infection (n = 9; infected for more than 6 months), Successfully treated (n = 13; undetectable viremia under HAART) and Elite controllers (n = 10; undetectable viremia without treatment). Multiparametric flow cytometry was used to analyze the memory phenotype (Naïve, CM, TM, EM, and Temra) and expression levels of CD160 and PD-1 on both total CD8 and HIV/CMV specific cells.

Patient population

	Time from infection	n	CD4 (cells/mm ³)	CD8 (cells/mm ³)	Log VL
Acute	2.8 (1.6 - 5.6)	12	360 (257 - 640)	728 (491 - 1990)	5.2 (4.13 - 6.59)
Chronic	11.7 (6.4 - 51.5)	9	494 (296 - 858)	717 (410 - 1081)	4.9 (4.0 - 5.39)
ST	86.1 (18.4 - 242.4)	13	563 (222 - 915)	631 (332 - 1120)	>1,7
EC seronegative controls	153.2 (116.7 - 240.6)	10	769 (445 - 1080)	976 (303 - 1514)	>1,7
		9			

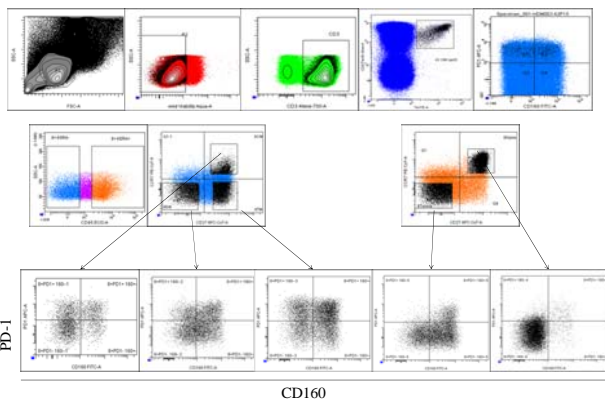


Figure 1: Gating strategy for the ex-vivo staining of PBMCs isolated from HIV-infected and uninfected donors.

High frequencies of HIV-specific CD8+PD1-160+ T cells are found in Elite Controllers (EC)

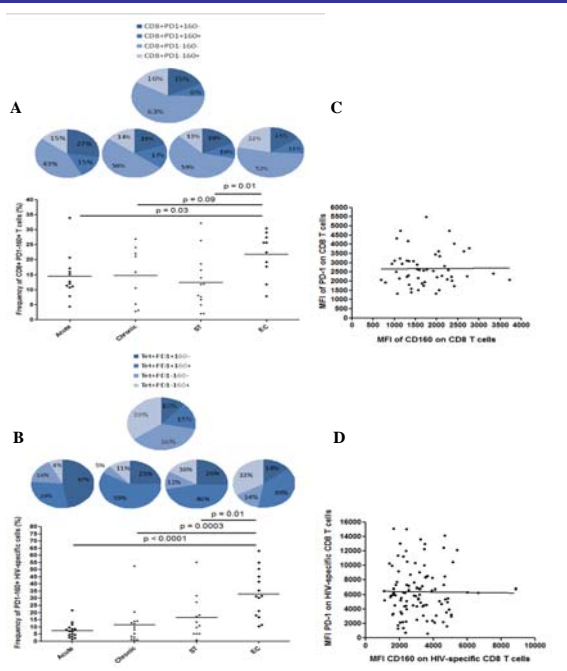


Figure 2: The frequency of PD1-160+ HIV-specific cells is significantly higher in Elite controllers. (A,B) We analyzed the relative distribution of 4 subsets of HIV-specific CD8 T cells: PD1+CD160-, PD1+CD160+, PD1-CD160- and PD1-CD160+. (C,D) MFI of PD-1 and CD160 was measured on both total and HIV-specific CD8 T cells and associations were drawn between both molecules.

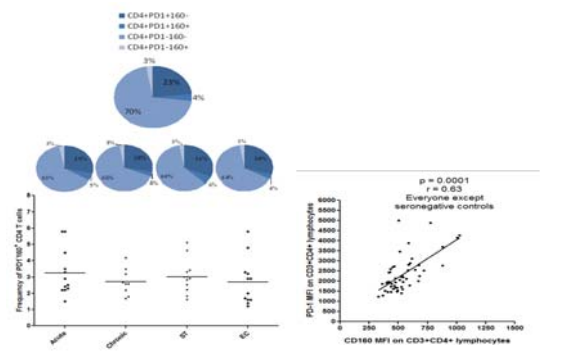


Figure 3: The relative distribution of CD4 T cells expressing PD-1 and/or CD160 does not differ between different stages of HIV disease.

Elite Controllers (EC) have similar frequencies of HIV and CMV-specific CD8+PD1-160+ T cells

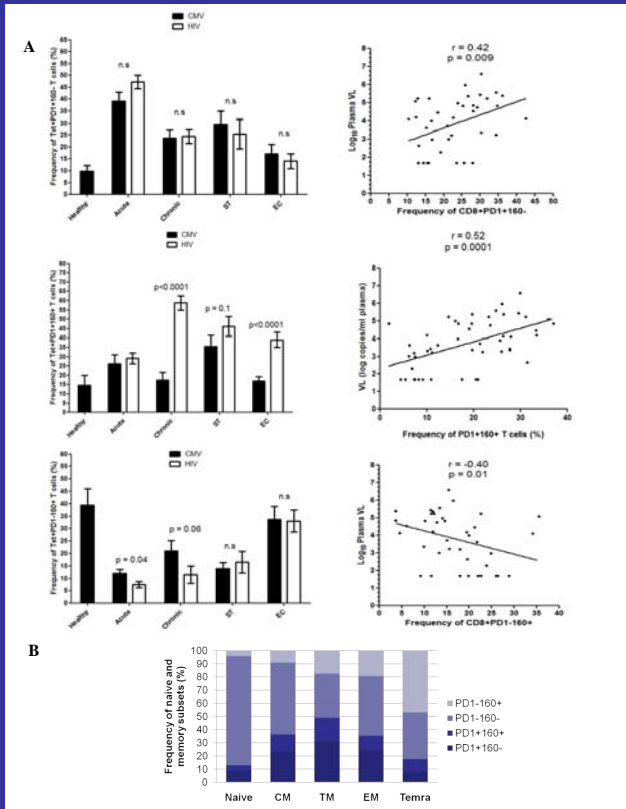


Figure 4: (A) Analysis of the distribution of PD-1 and CD160 expression on HIV and CMV-specific CD8 T cells in healthy and HIV infected individuals. (B) Memory phenotyping of the 4 different PD-1/CD160 subsets

CONCLUSIONS

- Taken together, our results show that Elite controllers are enriched in cells which express CD160 but not PD1. This cellular phenotype is predominant in CMV specificities from both healthy and HIV-infected individuals and negatively associates with viremia.
- There is a direct positive association between the expression levels of PD-1 and CD160 on CD4+ T.
 - No association was observed between the expression of these two molecules on HIV-specific CD8 T cells.
- The PD1-160+ phenotype is highly represented among cells which have a terminally differentiated phenotype (Temra: CD45RA+, CCR7-, CD27-)