P061 HIV Drug Therapy GLASGOW 2020

Contact: ltarancondiez@gmail.com

Increased levels of immune activation and exhaustion in vertically HIV-1 infected young adults

Tarancon-Diez L[1*], Carrasco I[2*], Vazquez-Alejo E[1], Jimenez de Ory S[2], Sainz T[3], Apilanez M[4], Rojo P[5], Guillén S[6], Ramos JT[7], Muñoz-Fernández MA[1ŧ], Navarro ML[2ŧ].

*[1]Laboratorio InmunoBiología Molecular, Hospital General Universitario Gregorio Marañón, Madrid, Spain. [2]Hospital General Universitario Gregorio Marañón, Paediatrics, Madrid, Spain. [3]Hospital Universitario La Paz, Madrid, Spain. [4]Hospital Universitario Donostia, Donostia, Spain. [5]Hospital 12 de Octubre, Madrid, Spain. [6]Hospital Universitario de Getafe, Madrid. [7]Hospital Clínico San Carlos, Madrid, Spain. *Equally contribution. ŧEqually contribution.*

Background: HIV-1 vertically infected children show irreversible immune damage associated with HIV-1 infection and early antiretroviral treatment (ART) exposure during immune system development. Most of these patients were born at the beginning of the HIV pandemic and are now reaching adulthood, and immunological data on this population remain scarce. The objective of this study is to assess the level of immune activation and imnunosenescence of HIV-1 vertically infected young adults compared to non-HIV-infected subjects.

Material and Methods: HIV-1 vertically infected patients (n=32) under suppressive ART for at least 5 years were selected from the Paediatric AIDS Research Network of Spain (CoRISpe) and cryopreserved samples were selected from the Spanish HIV BioBank. The HIV group was compared to a group of non-HIV-infected subjects (Healthy Donors, HD, n=28) matched by age and sex. General characteristics are shown in **Table 1**. The expression of activation, proliferation and exhaustion markers in CD4- and CD8-T cell subsets (defined by CD27 and CD45RA expression) and Natural Killer cells (NK) subsets (defined by CD56 and CD16 expression) was studied on peripheral blood mononuclear cells by multiparametric flow citometry using Gallios cytometer (Beckman Coulter).

Table 1. Patients' characteristics

	HIV (n=32)	HD (n=28)
Age (yrs)	24.4 [22.5-28.2]	26 [23.5-27]
Sex (male) n. (%)	12 (37)	9 (36)
% CD4+	35.5 [32-41.25]	37.8 [35.1-41.35]
% CD8+	36 [32.6-39]	20.3 [17.9-22.9]
n CD4+ cells/mm^3	794 [599-981]	
n CD8+ cells/mm^3	774 [622-938]	
Ratio CD4+/CD8+	1 [0.82-1.23]	
Nadir CD4+ cells/mm^3	198 [76-330]	
Age at ART initiation (months)	49 [14-70]	
Time since ART initiation (yrs)	20 [18-23]	
Time under viral control (yrs)	8 [7-10]	

Values are taken at sampling time-point. Continuous variables are expressed as the medians and interquartile ranges (IQR). Categorical variables are expressed as numbers and percentages.

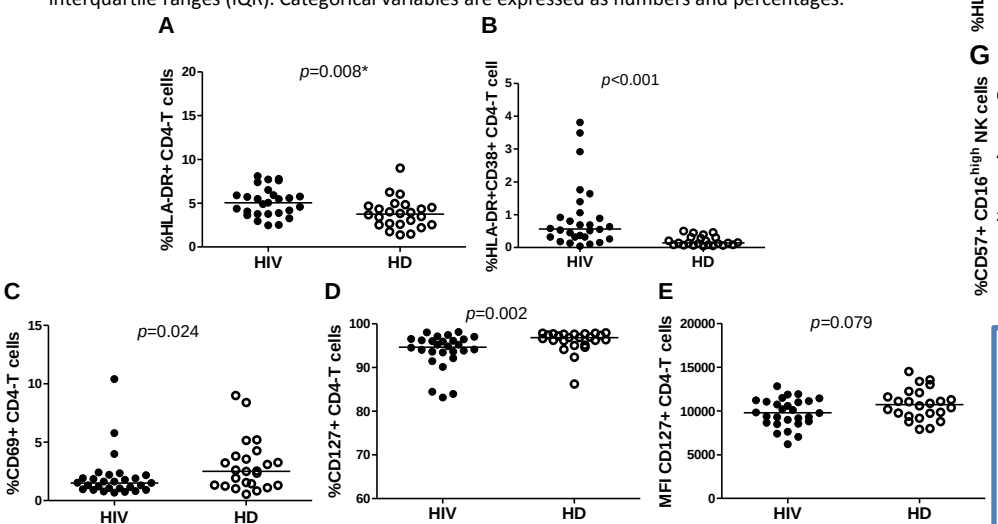

Figure 1. Activation and survival markers on CD4-Tcells. MFI: Median Fluorescence Intensity. Mann-Whitney U-test was used to compare groups. Similar results were found for CD8-T cell subsets.

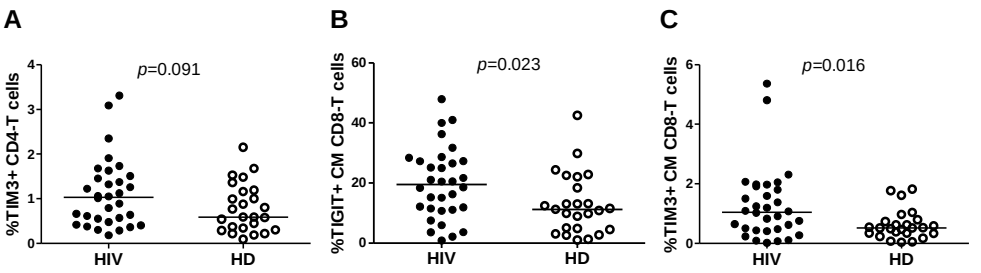

Figure 2. Exhaustion markers on total CD4-T cells and CD8-T memory subsets. CM: Central Memory (CD45RA-CD27+) CD8-T cells. Similar results for Effector Memory (CD45RA-CD27-) T-cells. Mann-Whitney U-test was used to compare groups.

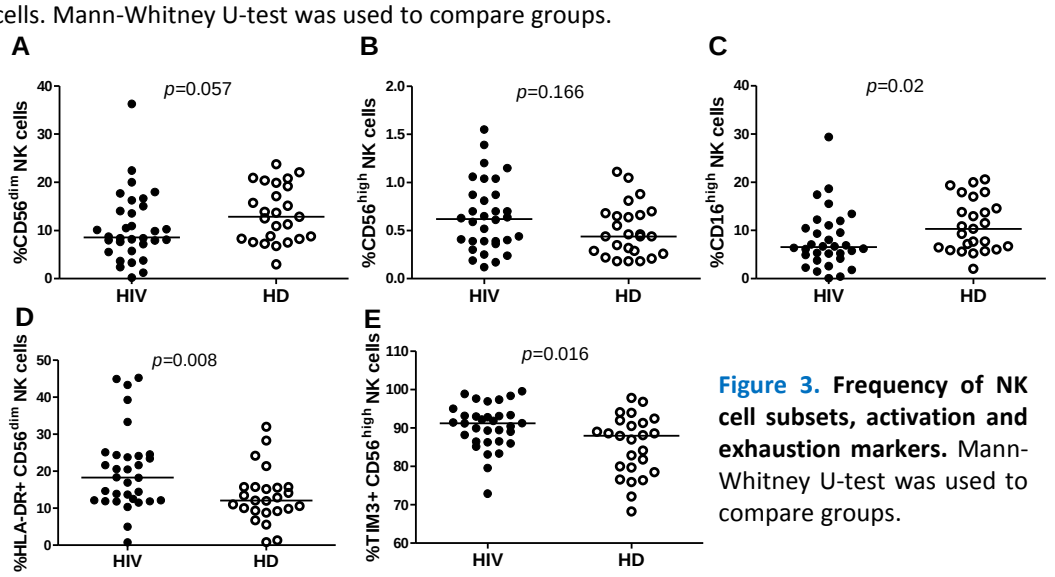

Figure 3. Frequency of NK cell subsets, activation and exhaustion markers. Mann-Whitney U-test was used to compare groups.

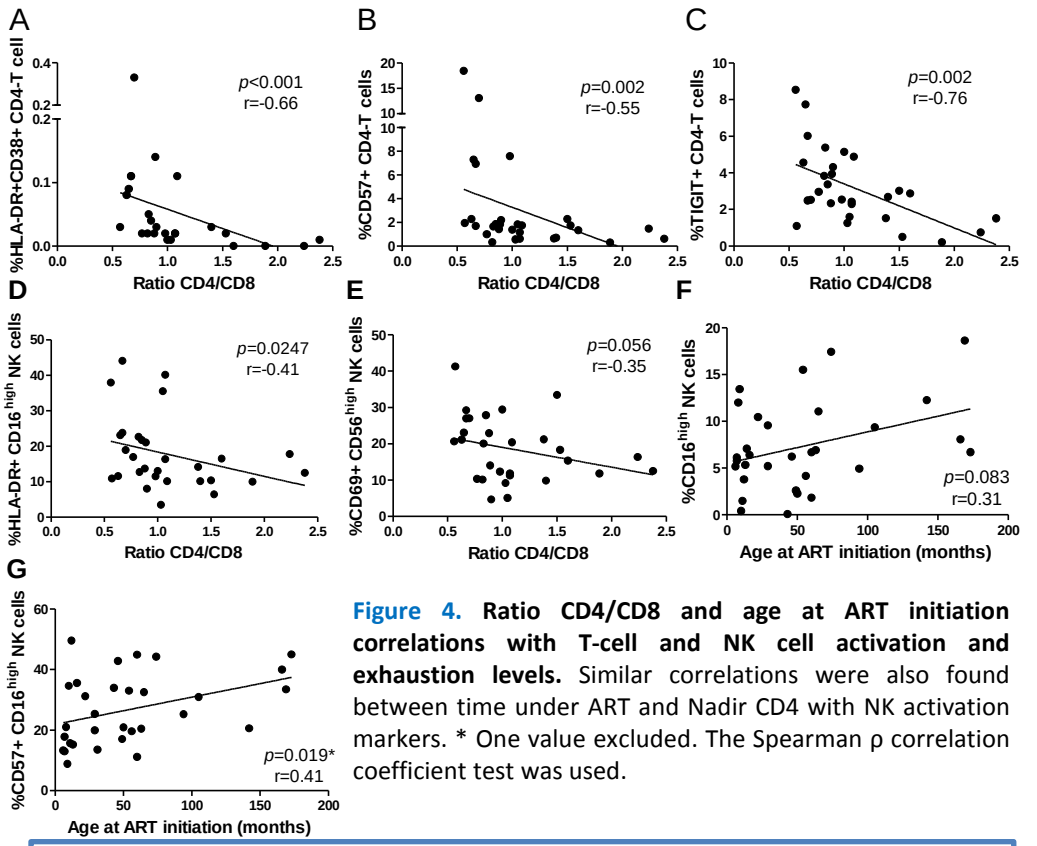

Figure 4. Ratio CD4/CD8 and age at ART initiation correlations with T-cell and NK cell activation and exhaustion levels. Similar correlations were also found between time under ART and Nadir CD4 with NK activation markers. * One value excluded. The Spearman ρ correlation coefficient test was used.

Conclusion: Vertical HIV-1-transmited infection deals with an irreversible immune damage not normalized once adulthood is reached, shown by increased activation and exhaustion marker levels in adaptive and innate immune components that is associated with clinical parameters including ratio CD4/CD8 and age at ART initiation.

Funding: Instituto de Salud Carlos III – Spanish Ministry of Science and Innovation: **PI19/01530**.