DENDRITIC CELLS CROSSTALK WITH FOLLICULAR CD8+ T-CELLS IN HIV-INFECTED LYMPH NODES

Poster 198

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Background /Aim

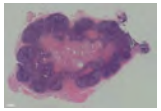
Plasmacytoid dendritic cells (pDCs) have been related with HIV spontaneous control. However, a deregulation mainly consisting in an aberrant IFN-I production lead to an inflammatory environment that could enhance HIV pathogenesis. It has been communicated that HIV provokes alteration in phenotype and location of CD8 T-cells within lymph nodes (LN). In a mouse model, a cooperative activity between pDCs and XCR1 dendritic cells (DCs) in order to effectively antigen cross-priming to CD8+T cells has been reported. However, the phenotype, function of pDCs and its interaction with other cell types in lymphoid tissues in relation with HIV-disease outcomes remain largely unknown

Methods

Seven inguinal LN samples prior to antiretroviral treatment onset (logViral Load (VL)= 4.6 (3.8-4.9) HIV-RNA copies/ml) were obtained from HIV-infected patients from Hospital Universitario Virgen del Rocio. PBMCs were obtained at the same point of LN biopsies. Cells were disaggregated, frozen and analyzed by multiparametric flow cytometry in a 30-parameters A-Symphony flow cytometer. A comprehensive analysis of DC, pDC and T-cell subset was performed.

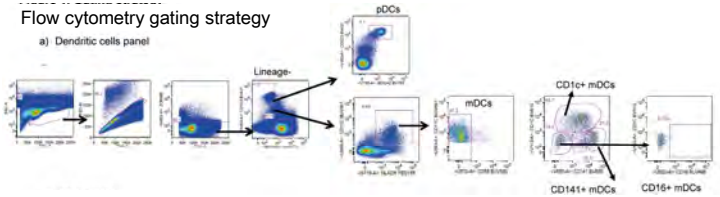
	Sex	Age (years)	Diagnosis T (months)	Nadir CD4 (cells/µL)	CD4 (cels/µL)	CD8 (cels/µL)	VL (log copies/mL)	CD4/CD8 ratio	HCV (Ant©HCV)
LN05	male	26	3,6	392	392	723	3,06	,54	Neg
LN08	male	23	1,56	415	428	591	4,68	,72	Neg
LN10	male	34	19,2	323	652	737	3,83	,88	Neg
LN12	male	36	6,36	333	487	1061	5,61	,46	Neg
LN13	male	31	23,4	312	378	918	4,97	,41	Neg
LN14	male	27	2,16	733	752	945	4,65	,80	Neg
LN16	male	29	0,96	356	376	544	4,73	,69	Neg

Results



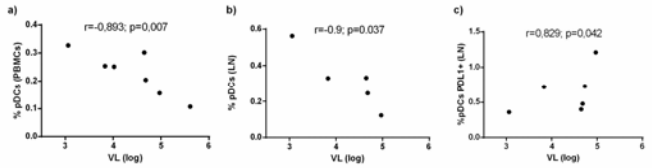
H&E lymph node

Flow cytometry gating strategy



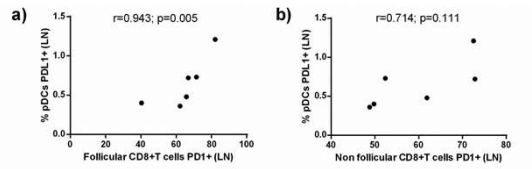
VL AND pDCs FREQUENCY IN LN

We confirm the inverse correlation between VL and the frequency of pDCs in peripheral blood previously found by our group and others (a). Herein we demonstrate that also the frequency of pDCs in LN negatively correlated with VL (b). Furthermore, VL positively correlated with the levels of pDCs expressing PDL1 in LN (c), suggesting that the higher VL evokes the more exhaustion of pDCs.



PD1-PDL1 AXIS BETWEEN FOLLICULAR CD8+T CELLS AND pDCs

We found a strong correlation between the percentage of pDCs expressing pDL1 and the levels of follicular CD8+T cells PD1+ (a). Of note, this correlation was not present neither between the levels of pDCs PD1+ and non-follicular CD8+T cell levels (b) nor with other myeloid dendritic cells expressing PDL1.

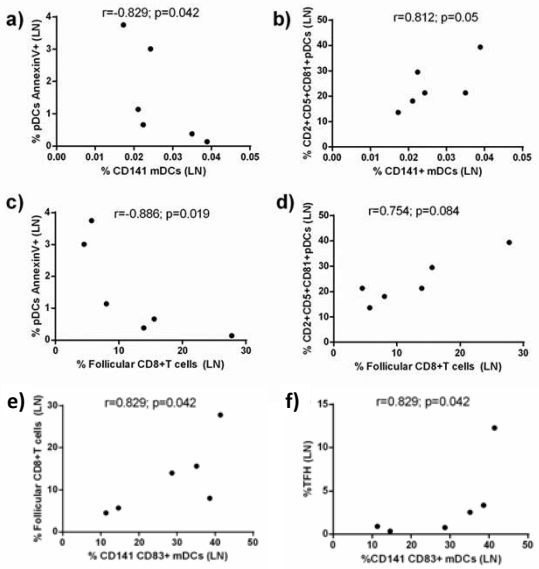


pDCS SURVIVAL, CD141 mDCS AND FOLLICULAR CD8+ T-CELL ASSOCIATIONS IN LN

The more frequency of CD141 mDCs and follicular CD8+ T-cells present in LN, the less pDCs exhibiting an early stage of apoptosis (r=-0.829, p=0.042 and r=- 0.886, p=0.019, respectively) (a,c).

We also found a direct correlation involving CD141 mDCs and follicular CD8+ T-cells frequency with %CD2+CD5+CD81+ pDCs (b,d). This pDC subset has been recently characterized and seem to be related with T-cell proliferation. It is the first time that this cells has been described in HIV scenario and in LN tissue.

In addition, we observed a direct correlation between mature CD83+CD141+mDCs and follicular CD8+T cell frequency and also with TfH frequency (e, f). CD83 is a key player in immune response regulation, specially T-cell proliferation



Conclusion

We explored a pDCs crosstalk with CD141+mDC and fCD8+T-cells, and its relation with fCD8 T-cell exhaustion in LNs of HIV-infected patients. This pathway may be a drug target that may enhance HIV-specific response within LNs, allowing the development of HIV curative strategies.
Further image analysis and functional assays are underway

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