Innate Immunity in the HTLV-1-Infection: IFN-Gamma levels are up-regulated and IFN-Alpha levels are down-regulated in the Early HTLV-associated myelopathy (HAM)

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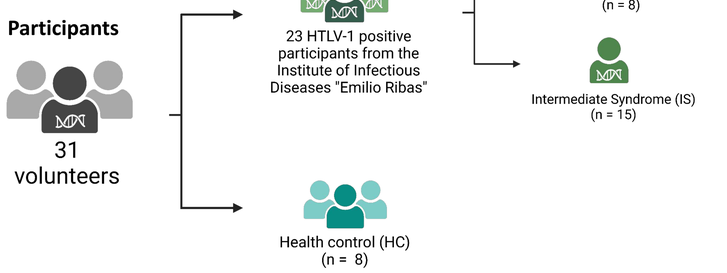
BACKGROUND

HTLV-1 infection is responsible for two aggressive diseases, leukemia and neuronal inflammation (HAM), in 5-10% of the chronically-infected asymptomatic carriers (AC). However, some infected individuals are not asymptomatic as they present minor symptoms that do not meet the criteria for HAM, which we named Intermediate syndrome (IS). To determine whether immune responses could discriminate IS from AC and healthy carriers (HC), which could then be used as biomarkers of disease progression, we analyzed in this study, the frequency of innate cells such as monocytes (cMono, intMono, and ncMono), dendritic cells (cDCs and pDCs), and NK cells and cytokine production, at steady state (spontaneous) or after stimulation (responsiveness).

METHODS

Participants



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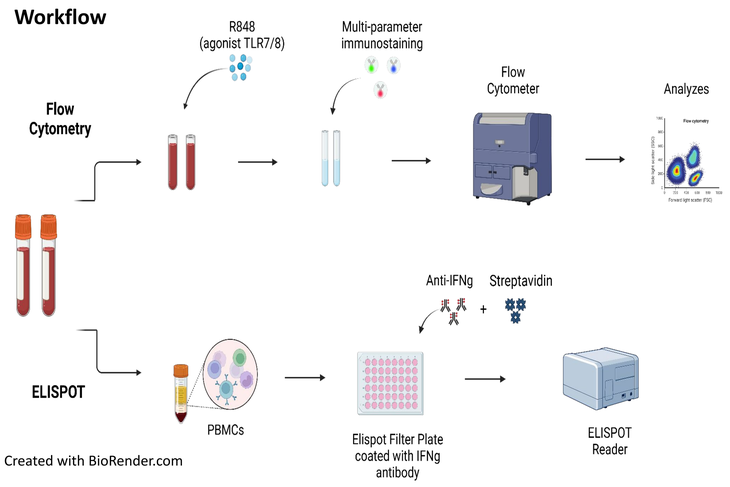
Workflow



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One-way ANOVA or Kruskal-Wallis statistical analysis was performed using the software GraphPad Prism 8.0 to compare parametric or nonparametric variables.

- **Patients in early stages of HAM showed a decreased responsiveness in pDC and increased in spontaneous IFN-g production by PBMCs.**
- **This finding could represent a signature of disease evolution.**
- **It may suggests that innate immunity impairment precedes the inflammation characteristic of HAM disease.**

RESULTS

31 volunteers were included (77% women and 23% men), with a median age of 56 years. No statistical difference was found in the cell subpopulations of the three groups. However, responsiveness of pDC cells, measured by IFN-α production (fig. 1a) was significantly reduced in the IS vs HC group (p=0.002), while the responsiveness of other DC such as cDC2 was not affected. Moreover, spontaneous IFN-γ production by PBMCs (fig. 1b) was increased in both asymptomatic and IS individuals compared to HC, with a statistical difference of p=0.0013 between HC and AC and p=0.0011 between HC and IS.

Table 1 – Main demographic data of study participants

Variable	Category	Total 31 (100%)	HC 8 (26%)	AC 8 (26%)	IS 15 (48%)	*p* value
Age (years) mean ± SD		56 (13,9)	48,5 (14,0)	49,9 (18,5)	57,8 (10,3)	0.2
Gender	Female	24 (77%)	6 (19,4%)	5 (16,1%)	13 (41,9%)	
	Male	7 (23%)	2 (6,5%)	3 (9,7%)	2 (6,5%)	

One-way ANOVA Test. HC: Health controls; AC: Asymptomatic Carriers; IS: Intermediate Syndrome;

CONCLUSIONS

Changes in innate and adaptive immunity are observed in HTLV-1 infected individuals compared to healthy donors regardless of their disease status. A decrease in the IFN-α-responsiveness of pDC and an increase of spontaneous IFN-γ production by PBMCs in IS compared to AC might be a signature of disease evolution to HAM.

ADDITIONAL KEY INFORMATION

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FIG. 1 Dendritic cells and peripheral blood of Intermediate syndrome (IS) patients present impaired response. a) Frequency of innate plasmacytoid dendritic cells in the clinical groups evaluated.
b) Interferon-gamma Spot forming cells of peripheral blood comparison between health controls, asymptomatic carriers and intermediate syndrome patients.

