HTLV-1 RETROVIRUS IS NOT DETECTED BY DENDRITIC CELLS BUT ALTERS THEIR RESPONSE TO A RESTIMULATION

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Background:
Human T lymphotropic virus 1 (HTLV-1) infection leads to chronic infection that remains asymptomatic in the vast majority of case, but is fatal in 5-10% of infected individuals who develop HTLV-1-associated diseases. Furthermore, immune dysfunctions have been repeatedly reported in asymptomatic HTLV-1 carriers, indicating that chronic infection induces systemic effects and hampers the ability of the immune system to respond adequately. Indeed, dendritic cells (DC) from infected individuals exhibit a defect in NF-κB-driven maturation suggesting a lower ability to initiate HTLV-1-specific T-cell responses, reminiscent of DC-induced tolerance. We aim to decipher how HTLV-1 induces this tolerant status of DC.

Methods:
Human monocytes obtained from healthy blood donors were differentiated into monocyte-derived DC (MDDC) and exposed to chronically infected T-cell lines as a model of primary infection. MDDC phenotype and responsiveness were monitored by flow cytometry, cytokine quantification and RNAseq analysis.

Results:
We showed that MDDC failed to mature after HTLV-1 exposure and were barely sensitive to a secondary stimulation through TLR4, with a decreased induction of MDDC maturation markers and TNF-α production, whereas IFN-I production after restimulation was not affected. MDDC's lack of responsiveness was independent from viral particles capture, IL-10 production by HTLV-1-infected T-cells or direct tight contact with infected cells.
RNAseq on MDDC exposed to HTLV-1-infected T-cells and restimulated or not identified several differentially regulated pathways. Among them, NF-κB and TNF-α signaling were downregulated in restimulated HTLV-1-exposed MDDC.

Conclusion:
Together, our results suggest a specific deregulation of MDDC signaling pathways after exposure to HTLV-1-chronically infected T-cell lines. Deep identification of these pathways is ongoing and will provide insights on how interaction of HTLV-1 with DC jeopardize their functions to shift towards a tolerant environment favorable to the chronic infection.

Disclosure of Interest Statement:
None