Enriched cell pathways associated with dysregulated miRNAs expression by HTLV-2 infection

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Background:
Human T-lymphotropic virus type 1 (HTLV-1) and type 2 (HTLV-2) both cause persistent infections, but they differ in clinical outcomes. Despite their strong genomic similarity, HTLV-1 is oncogenic whereas HTLV-2 has not been linked to malignancy. Comparative molecular analysis of HTLV-1 and -2, may help to understand the potential contribution of viral gene expression to their distinct pathogenicity. In this study, we aimed to identify cellular microRNA expression signatures associated with HTLV-2 infection to compare them with differentially expressed microRNAs in HTLV-1 infection transcriptomic datasets. We also investigated the potential implication of the deregulated miRNAs in the pathophysiology of HTLV diseases.

Methods:
micro-RNA analysis was performed in peripheral blood mononuclear cells from HTLV-2 infected subjects in comparison to healthy controls and HTLV-2 positive immortalized cells (BJABGu cell line) applying the Megaplex Pools protocol for 377 unique microRNAs. Enrichment analysis of targeted pathways was evaluated by using KEGG and Reactome databases. Deregulation of selected miRNAs targets was validated by real-time PCR and western blot analyses.

Results:
Eight miRNAs (125a-3p, 381-3p, 502-5p, 708-5p, 548d-5p, 548c-5p, 1-3p, 511-5p), were found to be significantly deregulated in both HTLV-2-infected cell populations. Applying enrichment analyses of the most significantly altered miRNA targets, we found that cytokine signaling (i.e. IL-17), as well as transcription factor pathways, were overrepresented. In this regard, of note, pathways associated with several miRNAs were enriched in RUNX family members. We validated the overexpression of RUNX-2 proteins through *in vitro* cell models. The molecular signature of deregulated miRNAs in HTLV-2 infected cells differed when compared to that of miRNAs deregulated by HTLV-1.

Conclusion:
Our findings shed light on the expression of specific miRNAs in HTLV infected cells, which may help to elucidate the host-virus interaction, opening the stage for future investigations on biomarkers of persistent infection.

Disclosure of Interest Statement: None