HTLV-1 INFECTED CELLS MODULATE TARGET CELLS AND VIRAL SPREAD VIA EXTRACELLULAR VESICLES

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Background:
Human T-cell Lymphotropic Virus Type-1 (HTLV-1) causes Adult T-cell Leukemia/Lymphoma and HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis. HTLV-1 infects about 10 million globally and its mechanisms are not fully understood. We have previously shown that Extracellular Vesicles (EVs) enhance viral spread, suggesting a role in HTLV-1 infection.

Methods:
EV populations (2K, 10K, 100K) from cell supernatants were isolated via differential ultracentrifugation. EV cargo was assessed and EV functionality was studied *in vitro* and *in vivo* and evaluated using fluorescent microscopy, immunoblotting, and RT-qPCR.

Results:
The 2K and 10K populations contained viral proteins (i.e., p19 and Tax), histones, and autophagy proteins (i.e., LC3 and p62). In an *in vitro* angiogenesis assay, 2K EVs caused tubule deterioration and damage. Astrocytes, neurons, and macrophages showed that EVs induce expression of cytokines involved in migration. The 2K and 10K EVs promoted cell-cell contact and enhanced viral transmission *in vitro* (T-cells, monocyte-derived dendritic cells, PBMCs) and *in vivo* (NOG mice).

Conclusion:
These data suggest that EVs enhance HTLV-1 infection and specific subpopulations (2K, 10K), may be responsible for pro-inflammatory cytokine secretion, tissue damage, and viral spread.

Disclosure of Interest Statement:
Nothing to disclose.