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.