Effect of Extracellular Vesicles (EVs) from HTLV-1 on Cell Proliferation via "Autocrine" Feedback Loop

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Background:
Up to 10 million individuals are infected with Human T-cell Lymphotropic Virus Type-1 (HTLV-1), which causes incurable leukemia/lymphoma and myelopathy/tropical spastic paralysis. We recently demonstrated that HTLV-1 cells release heterogeneous populations of Extracellular Vesicles (EVs) carrying viral cargo that induce cell-cell contact, triggering HTLV-1 spread. However, there is a gap of knowledge for the role of EV subpopulations in HTLV-1 infection.

Methods:
We separated subpopulations of EVs from HTLV-1 infected cells (2K, 10K, 100K, 167K (4 hours), 167K (16 hours)) via differential ultracentrifugation. EVs were labeled (i.e. BODIPY) and added to HTLV-1 cells and were visualized at 1, 6, 24, and 48 hours. Various inhibitors blocking receptor- or non-receptor-mediated EV uptake were used to examine the mechanisms of HTLV-1 EV uptake by parental cells.

Results:
Our data indicate differential uptake of EV subpopulations over time, with all EVs being taken up by 24 hours. EVs including 2K, 10K, and 100K mainly used receptor-mediated uptake (i.e. ICAM-1), whereas macropinocytosis and phagocytosis (i.e., non-receptor-mediated uptake) were routes of uptake of 2K EVs. Uptake of 167K EVs varied (i.e. clathrin- or caveolin-mediated endocytosis, and/or lipid raft-mediated internalization).

Conclusion:
Our data reveals that HTLV-1 infected cells are potentially "addicted" to their own EVs for self-proliferation. Further work is needed to identify the EV specific cargo that mediates the autocrine effect and contributes to survival of infected cells.

Disclosure of Interest Statement:
Nothing to disclose.