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

Al Sharif S1,2, Mensah G1, Kim Y1, Khatkar P1, Erickson J1, Jafari R4, Pinto DO3, Branscome H1, Kashanchi F1*

1Laboratory of Molecular Virology, George Mason University, VA, USA
2King Saud Bin Abdulaziz University for Health Sciences, Saudi Arabia
3Walter Reed Army Institute of Research, Center for Infectious Disease Research, MD, USA
4Clinical Research Institute, Urmia University of Medical Sciences, Urmia, IR

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.