Extracellular vesicles (EVs) from HTLV-1 infected cells possess subpopulation-specific malignant transformation effects upon uninfected cells.

Zachary Cuba[1], Sarah Al-Sharif[1], Jafari R[2], James Erickson[1], Heather Branscome[1], and Fatah Kashanchi[1]

[1] Laboratory of Molecular Virology, George Mason University, Manassas, VA, USA
[2] Clinical Research Institute, Urmia University of Medical Sciences, Urmia, IR.

Background
Human T-cell Leukemia Virus Type 1 (HTLV-1) is the causative agent of Adult T-Cell Leukemia/Lymphoma (ATLL) and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). Our lab has previously shown that extracellular vesicles (EVs) from HTLV-1-infected cells contain viral cargo and promote cell-to-cell contact when placed on uninfected recipient cells, enhancing HTLV-1 infectivity. However, a gap of knowledge exists as to whether certain subpopulations of EVs contribute to a transformed phenotype in ATLL samples.

Methods
Density-based ultracentrifugation was used to isolate 5 distinct subpopulations of HuT 102 EVs (2K, 10K, 100K, 167K (4 hours), 167K (16 hours)). Nanoparticle tracking analysis (NTA) and western blot were used to characterize EVs. EV functionality was assessed via several *in vitro* assays including EV labeling and uptake, flow cytometry/cell cycle, soft agar, and scratch assay.

Results
Our data highlights the phenotypic differences (i.e. size distribution, protein expression) in different subpopulations of HuT 102 EVs. Moreover, this data also points towards their differential functional effects on various cellular processes including cellular uptake in uninfected recipient cells, immortalization (i.e. cell cycle control), migration (i.e. epithelial to mesenchymal transition (EMT)), and transformation (i.e. anchorage independent growth).

Conclusion
Collectively, this data suggests that certain HuT 102 EV populations contribute to alterations in phosphorylation pathways and upregulation of EMT and may, therefore, be responsible for promoting malignancy. Some of the results on EV subtypes and the drugs used to inhibit their uptake will be discussed. Importantly, these findings highlight the potential for targeted therapeutics that could inhibit EV uptake to prevent or decrease a cancerous phenotype.

Disclosure of Interest Statement:
Nothing to disclose.