In-depth proteomic analysis of human T-cell leukemia virus type 1 particles reveals novel insights into virus-host cell interactions

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Background:

Human T-cell leukemia virus type 1 (HTLV-1) is an oncogenic human retrovirus that infects 15-20 million people globally and is the etiological agent of an adult T-cell leukemia/lymphoma (ATLL) as well as HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). In this study, we sought to gain deeper insights into how HTLV-1 usurps host cellular proteins to support virus replication. In particular, we examined cellular host proteins that were incorporated into virus particles in order to identify whether they were actively participating in virus replication.

Methods:

Tandem mass spectrometry of highly purified HTLV-1 virions produced from infected T-cells. Immunoblot analysis, subcellular protein localization, and cellular protein depletion studies were done to gain deeper insights into the role of cellular protein-encoding genes in HTLV-1 replication.

Results:

We identified ~1700 cellular proteins incorporated into virus particles, including proteins associated with the cytoskeleton, adhesion, signaling, intracellular trafficking, and the ubiquitination and immune response systems. For example, protein kinase C and casein kinase substrate in neurons protein 2 (PACSIN2), which is known to regulate morphogenesis and endocytosis of caveolae, was identified as being recruited into HTLV-1 particles. PACSIN2 has been reported to be important for virus replication and cell-to-cell spread with other human viruses. The role of PACSIN2 in HTLV-1 replication, along with other cellular proteins incorporated into virus particles, is currently being investigated.

Conclusion:

Our experiments have identified cellular proteins incorporated into HTLV-1 particles, including proteins having known roles in virus replication as well as proteins suspected as having significant roles in virus replication and infectious spread. Our ongoing studies seek to characterize novel cellular proteins and their roles in HTLV-1 replication and cell-to-cell spread. Our findings will help address current knowledge gaps in the field regarding virus-host cell interactions important for HTLV-1 replication, infectious spread and pathogenesis.

Disclosure of Interest Statement:

This research is funded by grants from the National Institutes of Health.