High-resolution structural analysis of capsid-capsid interactions reveals novel insights into HTLV-1 particle morphology

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Background:
During human T-cell leukemia virus type 1 (HTLV-1) infection, the Gag polyprotein is crucial for driving virus particle assembly and release. The capsid (CA) domain is the key determinant for Gag oligomerization through numerous protein-protein interactions. Despite strong homology in retroviral CA structures, HTLV-1 immature particles are unusual given their incomplete Gag lattice that include flat regions that are distanced from the viral membrane. While the human immunodeficiency virus type 1 (HIV-1) CA and that of other retroviral CA's have been well-characterized by high-resolution structural analysis, progress to date with HTLV-1 has been limited. This is in large part due to the difficulties in the propagation of HTLV-1 in culture. Here in this study, we sought to obtain a high-resolution structure for the HTLV-1 CA protein.

Methods:
Recombinant purified CA was assembled *in vitro* into two-dimensional CA lattice sheets and helical tubes. The two-dimensional sheets were subjected to cryo-electron microscopy/tomography. A hybrid crystal processing and single particle analysis has been used to generate a high-resolution map.

Results:
We observed crystal sheets that were well-ordered and had reflections up to 5.5 Å and exhibited a sixfold symmetry. To date, our evidence indicates that the sheets are comprised of CA protein organized in the mature lattice form. CA assembly was greatly enhanced by inositol hexaphosphate (IP6), a known co-factor for *lentivirus* assembly.

Conclusion:
The high-resolution analysis of CA-CA interactions has provided new insights into HTLV-1 particle assembly, and promises to provide deeper insights into particle morphology and reveal important clues into understanding the pleomorphic nature of HTLV-1 particle structure.

Disclosure of Interest Statement:

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