

Analysis of EV Signatures from HAM/TSP Patient CSF

Pleet ML¹, Welsh JA², Killingsworth B², Traynor T², Clauze A¹, Hughes R¹, Magana S¹, Monaco-Kushner M¹, Ngouth N¹, Ohayon J¹, Akahata Y¹, Jones JC², Jacobson S¹

¹ Viral Immunology Section, Neuroimmunology Branch, NINDS/NIH, Bethesda, MD, USA

² Translational Nanobiology Section, Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Background:

HTLV-1 can cause a progressive neuroinflammatory disorder in some infected individuals called HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Extracellular vesicles (EV) are released from virtually all cell types, and may package many inflammatory factors and, in the case of infection, viral components. We have shown that EVs from HTLV-1-infected cells can package Tax protein and sensitize recipient T-cells for an HTLV-1-specific immune response. Here, we characterize HAM/TSP cerebrospinal fluid (CSF) EVs to investigate the origins and numbers of EVs during disease.

Methods:

CSF EVs from patients with HAM/TSP (n=10), asymptomatic carriers (ACs; n=5), healthy volunteers (HVs; n=10), multiple sclerosis (MS; n=10), and other neurological diseases (n=14) were characterized by number (microfluidic resistive pulse sensing) and cellular origin (bead-based multiplex flow cytometry for specific cell surface markers). Statistical analyses were performed for cell-origin correlations and “fingerprints” of EV origin signatures were generated for each group.

Results:

In this pilot study, EVs from HAM/TSP CSF showed a significant increase in CD8 ($p<0.001$) and CD2 ($p<0.001$) compared to HVs and MS patients. AC CD8+ and CD2+ EVs had signals elevated compared to HVs, but less than HAM/TSP patients. Levels of CD8+ EVs in HAM/TSP CSF positively correlated with the numbers of CD8+ T-cells in the CSF ($p=0.008$). No significant differences in CSF EV number were found between groups.

Conclusions:

This pilot study indicates that CD8+/CD2+ EVs in HAM/TSP CSF are consistent with immunopathologically-mediated disease associated with CNS inflammatory CD8+ cells in HAM/TSP. Moreover, the potential of utilizing this workflow for CSF EV analysis to implicate cell types important in the pathology of neurological diseases may help point to the molecular mechanisms of disease and targeted therapies.

Disclosure of Interest Statement:

None