Immunopathogenic CSF TCR repertoire signatures in HAM/TSP.

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Background:
T-cell receptor (TCR) repertoire profiling in HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) may provide a more complete understanding of the pathogenesis of this disorder. In this study, we examined and characterized disease specific TCR signatures in cerebrospinal fluid (CSF) of patients with HAM/TSP compared to control cohorts.

Methods:
TCR-β libraries using unique molecular identifier-based methodologies were sequenced in paired peripheral blood mononuclear cells (PBMCs) and CSF cells from HAM/TSP patients and normal healthy donors (NDs). In addition, TCR-β repertoires were analyzed in HTLV-1 Tax11-19-specific $CD8^+$ T cells from PBMCs of HAM/TSP patients with HLA-A*0201.

Results:
Sequence analysis demonstrated that TCR-β repertoires in CSF of HAM/TSP patients were highly expanded and contained both TCR clonotypes shared with PBMCs and uniquely enriched within the CSF. In addition, we examined TCR-β repertoires of highly expanded and potentially immunopathologic HTLV-1 Tax11-19-specific $CD8^+$ T cells from PBMCs of HLA-A*0201 positive HAM/TSP and identified a conserved motif (PGLAG) in the CDR3 region. Importantly, TCR-β clonotypes of expanded clones in HTLV-1 Tax specific $CD8^+$ T cells were also expanded and enriched in the CSF of the same patient.

Conclusions:
These results indicate that exploring TCR repertoires of CSF and antigen-specific T cells may provide a TCR repertoire signature in virus-associated neurologic disorders.

Disclosure of Interest Statement:
Nothing to disclose.