**Immunopathogenic CSF TCR repertoire signatures in HAM/TSP.**

Satoshi Nozuma¹,², Yoshimi Enose-Akahata¹, Kory R. Johnson³, Maria Chiara Monaco¹, Nyater Ngouth¹, Abdel Elkahloun⁴, Joan Ohayon⁵, Jun Zhu⁶ and Steven Jacobson¹

1 Viral Immunology Section, Neuroimmunology Branch, National Institute of Neurological Disorder and Stroke, National Institutes of Health  
2 Department of Neurology and Geriatrics, Kagoshima University Graduate School of Medical and Dental Sciences  
3 Bioinformatics Section, National Institute of Neurological Disorder and Stroke, National Institutes of Health  
4 Comparative Genomics and Cancer Genetics Branch, National Human Genome Research Institutes, National Institutes of Health  
5 Neuroimmunology Clinic, National Institute of Neurological Disorder and Stroke, National Institutes of Health  
6 Mokobio Biotechnology R&D Center

**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 HLA-A*0201 positive 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.