NOVEL ASPECTS OF THE AUSTRALIAN HTLV-1C STRAINS

Damian Purcell, PhD

Viral infectious Diseases Theme leader, Peter Doherty Institute for Infection and Immunity, University of Melbourne, Melbourne, VIC, Australia

Human T-cell lymphotropic virus type-1 subtype-C (HTLV-1c) infects predominantly CD4+, CD8+ and ϫδ T-cells and to a lesser extent, B-cells, monocytes, and dendritic cells. HTLV-1c is endemic in remote indigenous Aboriginal communities where prevalence is often greater than 50%[1]. Peripheral blood mononuclear cell (PBMC) DNA samples were obtained following ethics approval and patient consent in first language. We sequenced the HTLV-1c genomes from 30 patients (Alice Springs Hospital, ASH) and examined the structure of HTLV-1c spliced mRNA. The involvement of HTLV-1c-infected T-cells in clinical pathogenesis was assessed in longitudinal analysis of 84 HTLV-1+ individuals using a digital droplet PCR (ddPCR) assay capable of quantifying the HTLV-1c proviral load (PVL) in total PBMC and in T-cells. The T-cell receptor V-beta locus (TCRβ) gene repertoire of HTLV-1c-infected cells from 22 patients was examined to test for antigen driven T-cell clonal expansion.

Comparison of Cosmopolitan (A) and Austral-Melanesian (C) HTLV-1 clades showed homology greater than 90% across the entire genome. However, the HBZ and p12/p8 coding regions exhibited considerable differences at both the nucleotide (12 and 18%, respectively) and amino acid levels (18 and 25%, respectively). There was no initiation codon at the expected position for p12/p8 and novel spliced mRNA may support expression of a p16 version of this protein with different functions. These features may contribute to the observed inflammatory pathogenesis and apparent low-rates of T-cell leukaemia which depends on HBZ. Indigenous Australians exhibited a wide PVL per T-cell ranging from $8x10^2$ – $5x10^6$ copies/10^6 T-cells and suggested expansion in myeloid cells. High PVL strongly associated with chronic inflammatory conditions of the lung, especially bronchiectasis, but the HTLV-1-associated myelopathy observed elsewhere was rare. Most common were skin and blood stream infections suggesting a subtle functional immunodeficiency[1]. Further studies are needed to examine the functions of HTLV-1c regulatory and accessory genes and to develop vaccines and antiviral drug treatments to combat HTLV-1c transmission. To this end an Aboriginal led academic consortium aims to research the scope and impact of HTLV-1c infections in Australia.

1. Einsiedel et al. MJA 2016