An investigation of the HIV Tat C31S and R57S mutation on peripheral immune markerlevels in South African participants: A pilot study

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The HIV transactivator of transcription (Tat) protein has a functional role in the neuropathophysiology of HIV-associated neurocognitive disorders (HAND). Pre-clinical studies have identified the Tat C30S and R57S mutations as crucial contributors to the immune activity and neurovirulence of HIV-1 subtype C (HIV-1C) infection. However, clinical studies on human samples are limited. This study investigated the association between peripheral blood immune markers and Tat sequence variation at positions 31 and 57. The immune markers (TYMP, CCL2, VEGF, MMP9, NGAL, and TGF-β1) were selected on evidenceof their link to key neuro-immune function and were measured using enzyme-linked immunosorbent assays. Sanger sequencing was used to sequence Tat exon 1. Fifty-two people living with HIV were included, of which fifty-one had the C31 or C31S mutation and forty-nine had the R57 or R57S mutation. Peripheral immune marker levels did not differ across the C31S and C31 groups (all $p > .05$). Peripheral TYMP and CCL2 levels were lower inthe R57S group compared to the R57 group ($p < .05$). This pilot study provides evidence thatthe Tat sequence variant which is largely present in HIV-1C (R57S) may account for the lower TYMP and CCL2 levels in HIV-1C infection. Future studies should investigate these signatures across larger cohorts to support the findings presented here.