HIGH LEVELS OF HIV RNA TRANSCRIPTS IN CSF CELLS DESPITE SUPPRESSIVE ART

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Background:
HAND persists despite suppressive cART, and we aimed to study HIV RNA transcripts in CSF cells and characterize CD4 T cells that may contribute to this CNS HIV reservoir, using high-dimensional flow cytometry and our highly-sensitive Double-R assay of HIV RNA transcripts.

Methods:
CSF cells and PBMC were compared by 18-colour flow cytometry. DNA and RNA were extracted in 20 paired samples of CSF and blood from HIV+ subjects on cART, with both plasma and CSF HIV RNA (Roche) <50 copies/ml. HIV-1 transcripts and DNA were determined by the Double-R πCode MicroDiscs assay, as copies/10^6 CD4. In vivo brain injury was assessed with MR spectroscopy in the frontal white matter (FWM) and posterior cingulate cortex (PCC).

Results:
CSF cells were 91% memory T cells, comprised equally of memory CD4 (median 3,605 cells recovered) and CD8 T cells (3,507). Other CSF cells were 3.1% CD14+CD16+ monocytes, 2.0% NK cells and 0.4 % B cells. Memory CXCR3+CD49d+integrinß7- cells were 76% of CD4 T cells in CSF (vs 17% in PBMC); 51% were CCR5+ (vs 16%); and 18% expressed CD38 and/or HLA-DR activation markers (vs 11%). 18/20 patients' CSF cells had significantly higher cell-associated HIV-1 RNA transcripts vs PBMCs (8,331 vs 680; $p<0.0001$), but levels were significantly correlated between CSF cells and PBMC ($r=0.46$; $p=0.029$). 16/20 patients also had significantly higher HIV-1 DNA levels in CSF cells vs PBMC (median 3,940 copies/10^6 cells vs 885; $p<0.0001$). CSF transcripts were inversely correlated with the neuronal integrity biomarker N-acetyl aspartate in FWM ($p=0.04$) and PCC ($p=0.055$).

Conclusion:
CSF cells have high transcription activity despite ART, most likely in the predominant CXCR3+CD49d+integrinß7-CCR5+ memory CD4+T cells. Ligands for CXCR3+ cells, especially IP-10, likely induce trafficking of circulating infected CD4 T cells into the CNS. Therapies targeting transcription should be developed, to reduce compromised neuron integrity.

Disclosure of Interest Statement:
K.S. receives research funds from Denka Co. Ltd. K.S. is the original inventor under WO2018/045425 (PTC/AU2017/050974) patent, titled "Methods of detecting Lentivirus" of HIV-1 detection targeting "R" region.