CNS HIV BEARS ENVELOPE MARKERS CONSISTENT WITH T-CELL ORIGIN IN THE FACE OF ART

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BACKGROUND

One line of evidence that the CNS may be a source for HIV in the face of ART is cerebrospinal fluid (CSF) escape, where HIV is suppressed in the blood but detectable in the CSF. However, it is unclear if CSF HIV is CNS restricted by infecting a cell type such as microglia or is produced by T cells, capable of migrating in and out of the CSF compartment.

Infection state	n (F/M)	Age (IQR)	VL[1] CSF (IQR)	VL Plasma (IQR)	CD4 count (IQR)	Year ART (IQR)	Fraction co-infect
CSF Escape	14 (7/7)	38 (33-41)	3795 (1210-24290)	<40	474 (389-636)	2.5 (1.2-6.5)	0.28
Suppressed	49 (32/17)	34 (30-41)	<40	<40	485 (152-707)	2.3 (0.9-5.7)	0.33
Viremic	59 (37/22)	33 (28-38)	3615 (173-23580)	19551 (1929-62631)	215 (94-399)	1.0[2] (0.08-4.2)	0.39

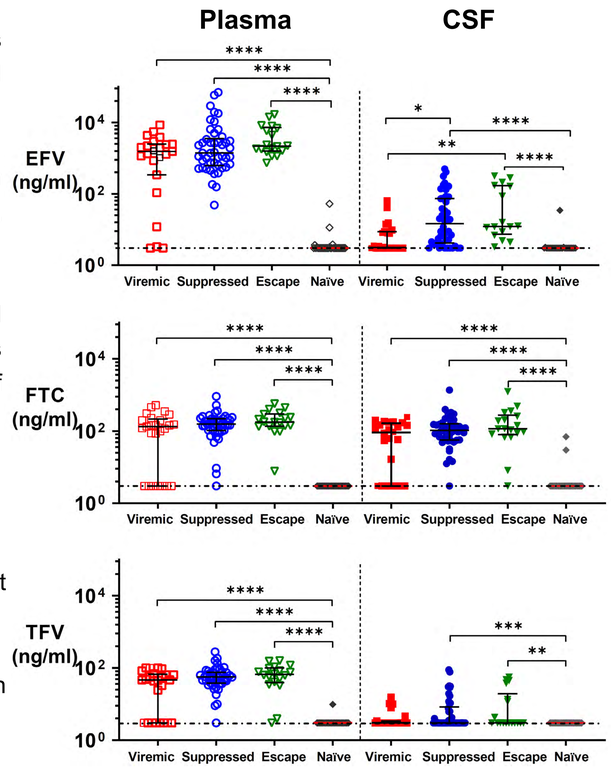
[1] Viral load in copies/ml, limit of detection of 40 copies/ml. [2] Of viremic participants on ART

METHODS

- Collected blood and CSF from 122 South African participants indicated for lumbar puncture and quantified viral load and antiretroviral drugs concentrations in blood and CSF.
- Determined CD26 and CD36 surface marker expression on CD3 gated PBMCs, human monocyte derived macrophages, and human microglia discarded from the field of surgery.
- Used anti-CD26 and CD36 virion binding followed by viral load assay to determine the ratio of cellular markers expressed on virions of participants on first line regimen of efavirenz (EFV), emtricitabine (FTC), and tenofovir (TFV).

RESULTS

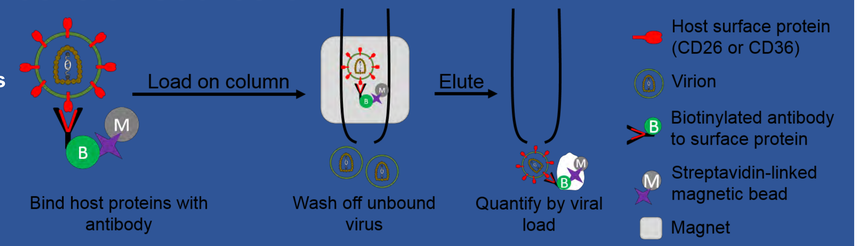
- 22% of participants from KwaZulu-Natal had CSF escape.
- ART levels of EFV, FTC, and TFV in blood or CSF not predictive of CSF escape.
- CD36 but not CD26 was expressed on the surface of human macrophages and microglia, differentiating them from T cells.
- Virion CD26/CD36 signature from *in vitro* infection could differentiate macrophages vs. T cells as viral source.
- HIV from CSF escape participants showed a similar CD26/CD36 ratio to T cell but not macrophage derived virus.



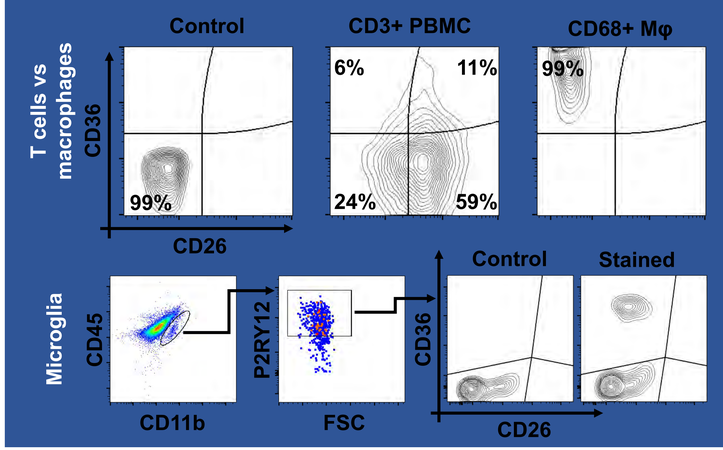
Medians and IQR of EFV, FTC, and TFV in the plasma (left) and CSF (right) in individuals who were viremic (red squares), suppressed (blue circles), showed CSF escape (green inverted triangles), or reported as treatment naïve (grey diamonds). Horizontal dotted line is detection limit.

Determination of cellular source of HIV

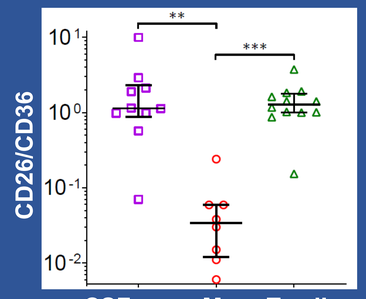
CD26/CD36 quantified on virions by binding to column linked anti- CD26 or CD36 Ab followed by elution and viral load.



Cell surface staining shows CD36/CD26 differentiates between T cells vs macrophages and microglia



CD26/CD36 on HIV from CSF escape matches T cell derived virus



CSF from 10 CSF escape participants (left) was divided and half applied to column with anti-CD26 and the other to column with anti-CD36. Ratio of virions bound by each column was compared to ratios from in vitro infected MDMs (middle) or PBMC (right).

CONCLUSIONS

- CSF escape was common in KwaZulu-Natal participants on ART, with CSF viral load similar to viremic participants.
- There was no association of CSF escape with lowered CSF or plasma ART levels, though past episodes of treatment interruption cannot be ruled out.
- HIV detected in the CSF was consistent with a predominantly T cell origin based on the ratio of T cell to macrophage markers on virions.
- The consequences of CSF escape for stroke, depression, and cognitive impairment is yet to be determined.

References

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