HIV-1 BURDEN IN PERIPHERAL BLOOD AND GUT CD4+ T CELLS EXPRESSING CD30 AND CD32

Louise E. Hogan[1], Joshua Vasquez[1], Kristen S. Hobbs[1], Emily Hanhauser[1], Brandon Aguilar-Rodriguez[1], Cassandra Thanh[1], Erica A. Gibson[1], Alexander B. Carvidi[1], Louis C. B. Smith[1], Ma Somsouk[2], Daniel R. Kuritzkes[3], Steven G. Deeks[4], Timothy J. Henrich[1]

[1] Division of Experimental Medicine, University of California San Francisco, San Francisco, CA, 94110; [2] Division of Gastroenterology, Department of Medicine, University of California San Francisco, San Francisco, CA, 94110; [3] Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115; [4] Positive Health Program, Department of Medicine, University of California San Francisco, San Francisco, CA, 94110

University of California San Francisco

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Introduction: Identification of specific, cell-surface markers of residual HIV infection is a top research priority. We studied CD30 (TNF superfamily receptor) and CD32 expression in blood and gut-associated lymphoid tissue (GALT), determined the HIV burden within CD4+ T cells expressing these markers, and evaluated response to *ex vivo* anti-CD30 therapy.

Methods: CD4+ T cells from blood or gut tissue were sorted based on expression of CD30 and CD32 followed by quantification of cell-associated HIV-1 DNA and RNA. *In situ* HIV RNA hybridization studies were performed on GALT to co-localize CD30 and HIV RNA. PBMC from ART-suppressed individuals were co-cultured in the presence of the cytotoxic antibody-drug-conjugate (ADC), brentuximab vedotin, an approved cancer therapy that targets CD30.

Increased Frequency of CD30+CD4+ T Cells in HIV-Infected Individuals

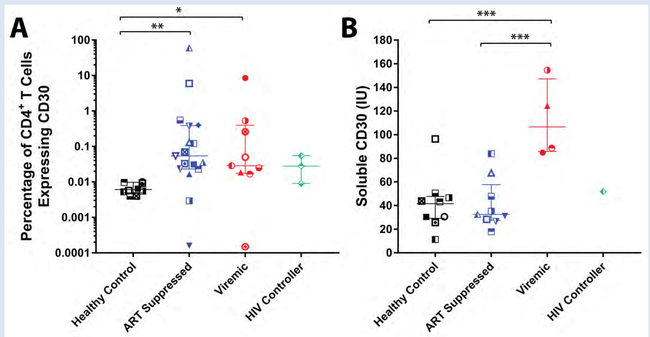


Fig 1. Percentage of CD4+ T cells expressing CD30 was higher in both ART suppressed and viremic individuals compared with healthy controls. Soluble (s)CD30, however, was elevated only in viremic participants.

HIV is Enriched in CD30+CD4+ T Cells

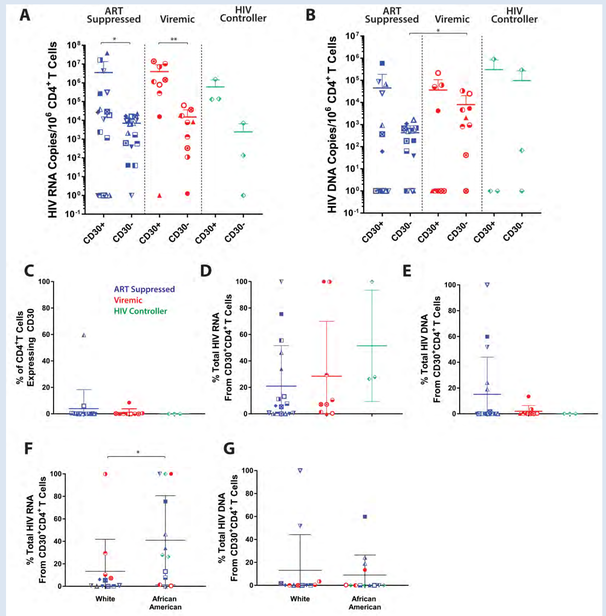


Fig 3. HIV-1 RNA is significantly enriched in CD30 expressing cells from ART suppressed donors (A, p=0.008) and viremic donors (p=0.007). (**C**) The contribution of CD30+CD4+ T cells to total CD4+ T cell population, and the contribution of HIV-1 RNA **(D)** and DNA **(E)** from CD30+CD4+ sorted cells to total HIV-1 RNA and DNA burden in CD4+ T cells, are shown. The percentage of total HIV-1 RNA **(F)** but not DNA **(G)** found in CD30+CD4+ T cells was significantly higher in African American than white participants (p=0.0103).

HIV RNA and DNA in CD30+ & CD32+ Rectal CD4+ T cells

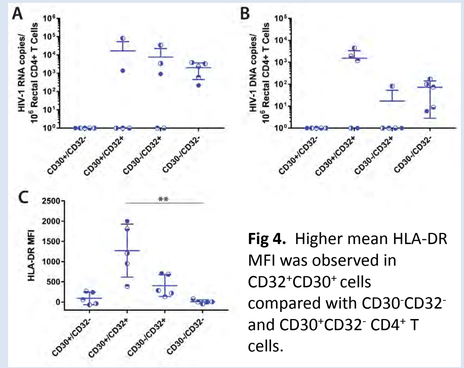


Fig 4. Higher mean HLA-DR MFI was observed in $CD32^+CD30^+$ cells compared with $CD30^-CD32^-$ and $CD30^+CD32^-$ $CD4^+$ T cells.

Anti-CD30 Treatment Reduces HIV DNA *Ex Vivo*

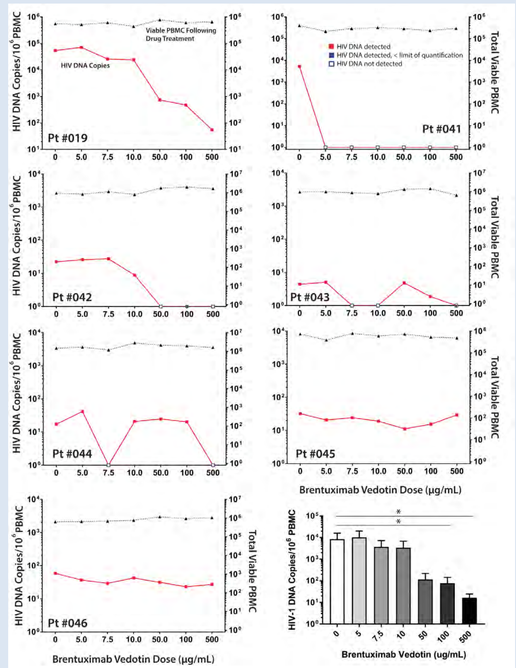


Fig 6. *Ex vivo* treatment with brentuximab vedotin led to reductions in cell-associated HIV-1 DNA, despite no change in viable cell numbers.

CD30 & HIV RNA Co-Localize in GALT

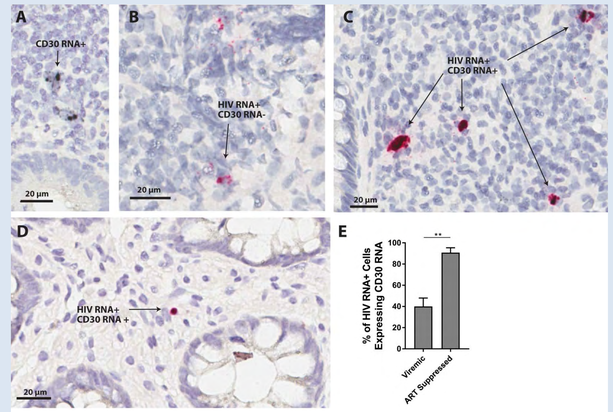


Fig 5. *In situ* chromogenic hybridization staining of HIV-1 RNA (pink) and CD30 RNA (black) was performed in ileum and rectum from HIV-1-infected individuals. Less than 0.1% of uninfected GALT cells expressed CD30 RNA (**A**). Although HIV-1 RNA^+ staining alone was identified in sections from GALT from viremic HIV-1-infected individuals (n=3) (**B**), 33% of HIV-1 RNA^+ cells also expressed CD30 (**C**). In GALT from ART-suppressed individuals (n=3), 88% of all HIV-1 RNA positive cells co-expressed CD30 (**D**). Percentages of HIV-1 RNA^+ expressing CD30 RNA are shown in (**E**).

CD30+CD4+ T Cells are of TM/EM Phenotype and Express PD-1

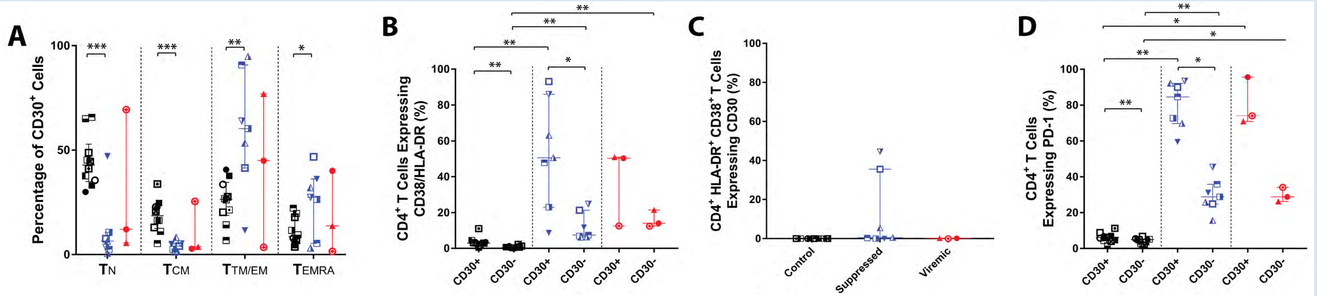


Fig 2. (**A**) The highest frequency of $CD30^+$ T cells observed in HIV-1-infected individuals were of transitional/effector memory phenotype. Despite significant increases in $CD30^+$ cells expressing CD38/HLA-DR (**B**), there were no significant differences in the frequency of CD30 expression in CD38/HLA-DR-expressing $CD4^+$ T cell populations (**C**). $CD30^+CD4^+$ T cells from viremic and ART suppressed participants expressed high levels of PD1 (**D**), but very few $PD1^+$ T cells expressed CD30.

Conclusions

- **CD30 expression is elevated in HIV-infected individuals regardless of ART use.**
- **CD30 expression appears to be a marker of residual HIV-1 transcriptional activity in the setting of ART in blood and gut tissue.**
- **Brentuximab vedotin (anti-CD30 ADC) is capable of reducing HIV-1 DNA burden *ex vivo*.**
- **Further investigation is warranted to determine the efficacy of targeting CD30 *in vivo* as a potential therapeutic target.**

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