Steady state and Post-vaccination TFH Dynamics in HIV Patients Treated with cART

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Introduction

- Persons with HIV/AIDS have significant morbidity/mortality due to influenza virus and are thus targeted for prevention through immunization[1]
- However, despite numerous reports on post-immunization antibody titers[2,3], the effects of vaccination on the lymphoid tissue cellularity and local virus reactivation have not yet been explored in HIV+, virologically suppressed patients on cART
- In this study we assessed the effect of trivalent seasonal influenza vaccination on the dynamics of tissue-resident TFH and B cells

Methods

- Lymph node (LN) -derived cells and tissues from healthy controls and virologically suppressed HIV+ subjects were obtained pre- and post- vaccination and analyzed by polychromatic flow cytometry (12 colour) and multicolour confocal imaging
- Influenza -specific antibody titers were measured by hemagglutination inhibition assay
- The effect of influenza vaccination on viral dynamics was determined in sorted LN-CD4 T cell populations by quantifying actively transcribing virus using PCR-based assays
- Fluidigm gene expression analysis was performed to assess the effect of vaccination on the transcriptional profile of tissue resident CD4 T cell subpopulations

Results

Figure 1. Gating strategy for T-cell follicular helper cell (TFH) characterization in LNMC suspensions

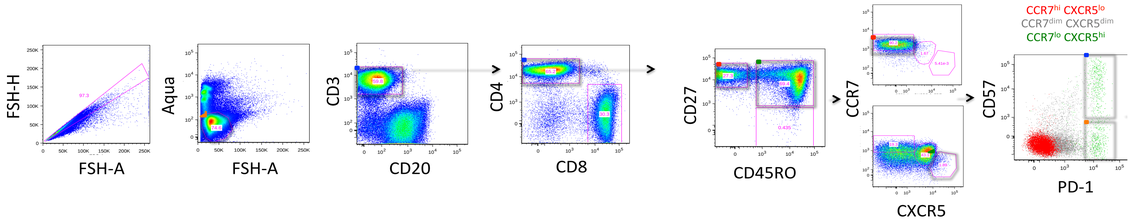


Figure 2. TFH are enriched in HIV+ cART LNs compared with HIV- pre-vaccination

Pre-vaccination TFH frequencies as determined by flow cytometry and IgG titers and frequency post-vaccination

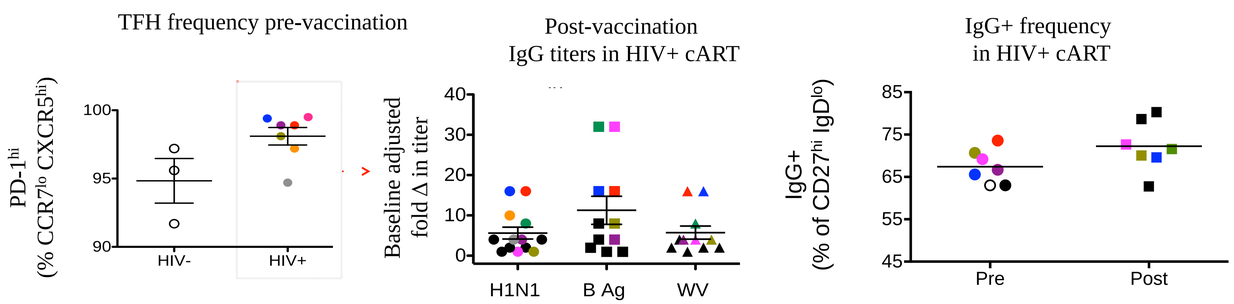


Figure 3a. Vaccination decreases the frequency of TFH in HIV+ cART LNs

TFH and TFH CD57 subpopulation frequency pre- and post-vaccination as determined by flow cytometry

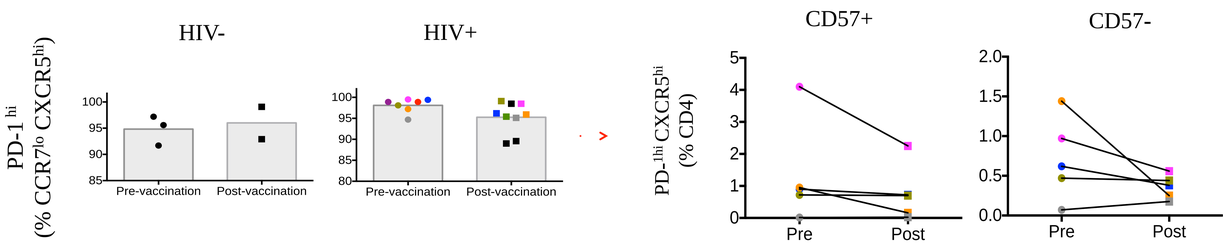


Figure 3b. Vaccination decreases the frequency of TFH in HIV+ cART LNs

Histocytometric analysis

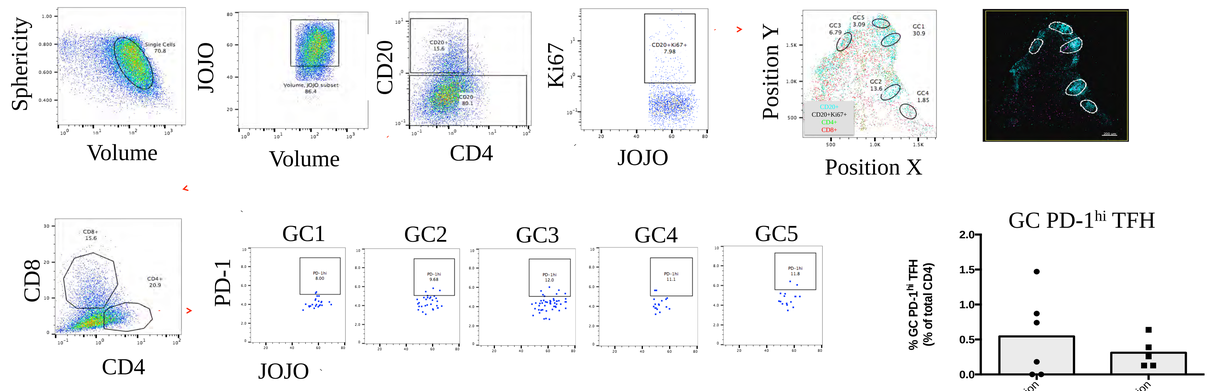


Figure 4. Vaccination decreases the amount of actively transcribing virus within the PD-1hi CD57+ and PD-1hi CD57- TFH subpopulations

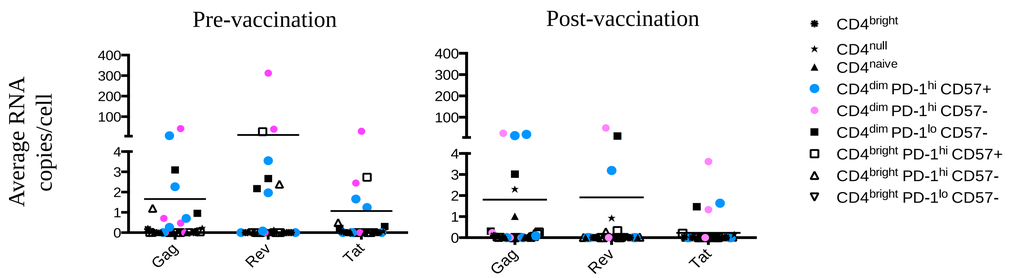
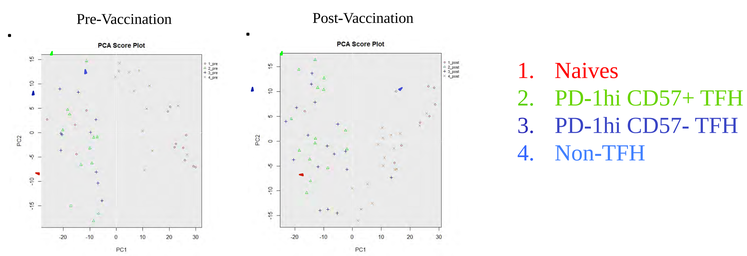


Figure 5. Principal component analysis (PCA) of Fluidigm gene expression data in TFH populations pre- and post-vaccination



Conclusions

- We show that TFH are enriched within HIV+ cART LNs pre-vaccination compared to HIV-. This is especially true for HIV+ patients mounting the strongest influenza-specific antibody responses
- We also show that vaccination, in addition to altering the gene expression signatures of TFH at two weeks post-vaccination, lowers the frequencies of tissue resident TFH and level of active HIV RNA transcription. The latter warrants further investigation as it could suggest a cause-effect relationship

References

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3 Parmigiani, A. *et al.* Impaired antibody response to influenza vaccine in HIV-infected and uninfected aging women is associated with immune activation and inflammation. *PloS one* **8**, e79816, doi:10.1371/journal.pone.0079816 (2013).