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Immune Activation Impairs Yellow Fever Vaccine Efficacy in HIV-infected Patients

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Background

- Yellow Fever Vaccine (YFV) induces **weaker and less durable responses** in HIV-infected individuals
- **Chronic immune activation may impair immune responses to YFV in HIV-uninfected individuals** (Muyanja E. et. al., J Clin Invest. 2014 Jul;124(7):3147-58)
- **Low CD4/CD8 ratio may reflect immune activation in treated HIV patients, but its association with strength and duration of vaccine responses is unclear**

Methods

- **HIV-infected and HIV-uninfected** Brazilian participants who received a **single prior YFV dose** were enrolled
- We excluded participants with diabetes, chronic liver, renal, or rheumatologic diseases, prior cancer (except Kaposi Sarcoma) or immunosuppressive therapy
- **All HIV-infected participants were ART-suppressed**

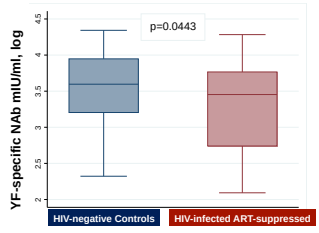
Table 1: Characteristics of participants*

	HIV-negative Controls N=58	HIV-infected, ART-suppressed N=34	p-value§
Age – years	38 (29-48)	46 (41-49)	0.088
Male gender - no. (%)	17 (29)	27 (79)	<0.001
Time since YF vaccine - months	69 (35-131)	41 (25-119)	0.156
AE after YF vaccine – no. (%)	12 (21)	3 (9)	0.158
CD4+ T count† – cells/mm^3	1120 (945-1308)	790 (603-956)	<0.0001
CD4+/CD8+ ratio†	1.8 (1.3-2.5)	0.7 (0.5-1.2)	<0.0001
HIV viral load <40 cop/ml – no.(%)	-	34 (100)	-

HIV, human immunodeficiency virus; ART-suppressed, antiretroviral therapy-suppressed with plasma HIV RNA level <50 copies/ml; YF,Yellow Fever; and AE;adverse events.
* Continuous variables are presented as medians and interquartile ranges.
§ Calculated using Wilcoxon rank-sum test for continuous variables and Chi-squared or Fisher's exact test for categorical variables
† Only available on 49 controls.

Results

Figure 1: NAb titers were significantly lower in HIV-infected than HIV-uninfected participants



Difference in NAb titers to YF remained significantly lower after adjustment for age, gender, and time since vaccination (p=0.024).

Figure 2: Time since vaccination is inversely correlated with YF NAb Titers in HIV-infected, but not in –uninfected participants

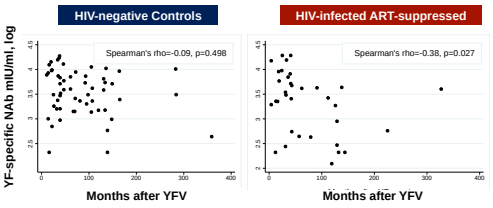
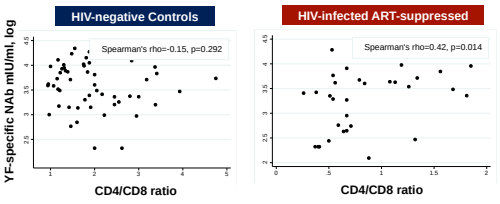


Figure 3: CD4/CD8 Ratio is positively correlated with YF NAb Titers in HIV-infected, but not in –uninfected participants



- **CD4⁺ T cell count** was **not correlated with YF NAb titers** in either HIV-uninfected (Spearman's rho=0.06, p=0.686) or ART-suppressed HIV-infected individuals (Spearman's rho=-0.11, p=0.519)

Conclusions / Implications

- Treated HIV-infected individuals appear to have **impaired and less durable neutralizing antibody responses to YFV** than HIV-uninfected individuals, which were **associated with lower CD4⁺/CD8⁺ ratio, but not with CD4⁺ T cell count**
- **Low CD4⁺/CD8⁺ ratio may be a better surrogate for functional immune defects than the CD4⁺ T cell count in treated HIV infection**
- **Booster vaccination for YF may be required for HIV-infected individuals**

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