Pulmonary tuberculosis disease enhances HIV-1 antibody responses

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BACKGROUND

Mycobacterium tuberculosis (TB) is an integral component of complete Freund's adjuvant which is known to augment antibody production. We hypothesized that active TB disease enhances the development of HIV-1 broadly neutralizing antibodies (bnAbs) in people living with HIV-1.

METHODS

We compared anti-HIV-1 antibody response among treatment-naive plasma samples from 15 HIV-1 patients with active pulmonary TB (HIV-1/TB) and 16 HIV-1 only infected individuals. Ability to inhibit 12 different tier 1 and 2 HIV-1 variants of diverse subtypes in the TZM-bl neutralization assay was used to estimate a neutralization breadth and potency (BP) score. Total IgG and cytokine levels were estimated using multiplex Luminex based assays. Neutralization heatmaps were used to identify potential targeted HIV-1 envelope epitopes. Comparisons were done using the Wilcoxon rank-sum and Fischer's exact tests.
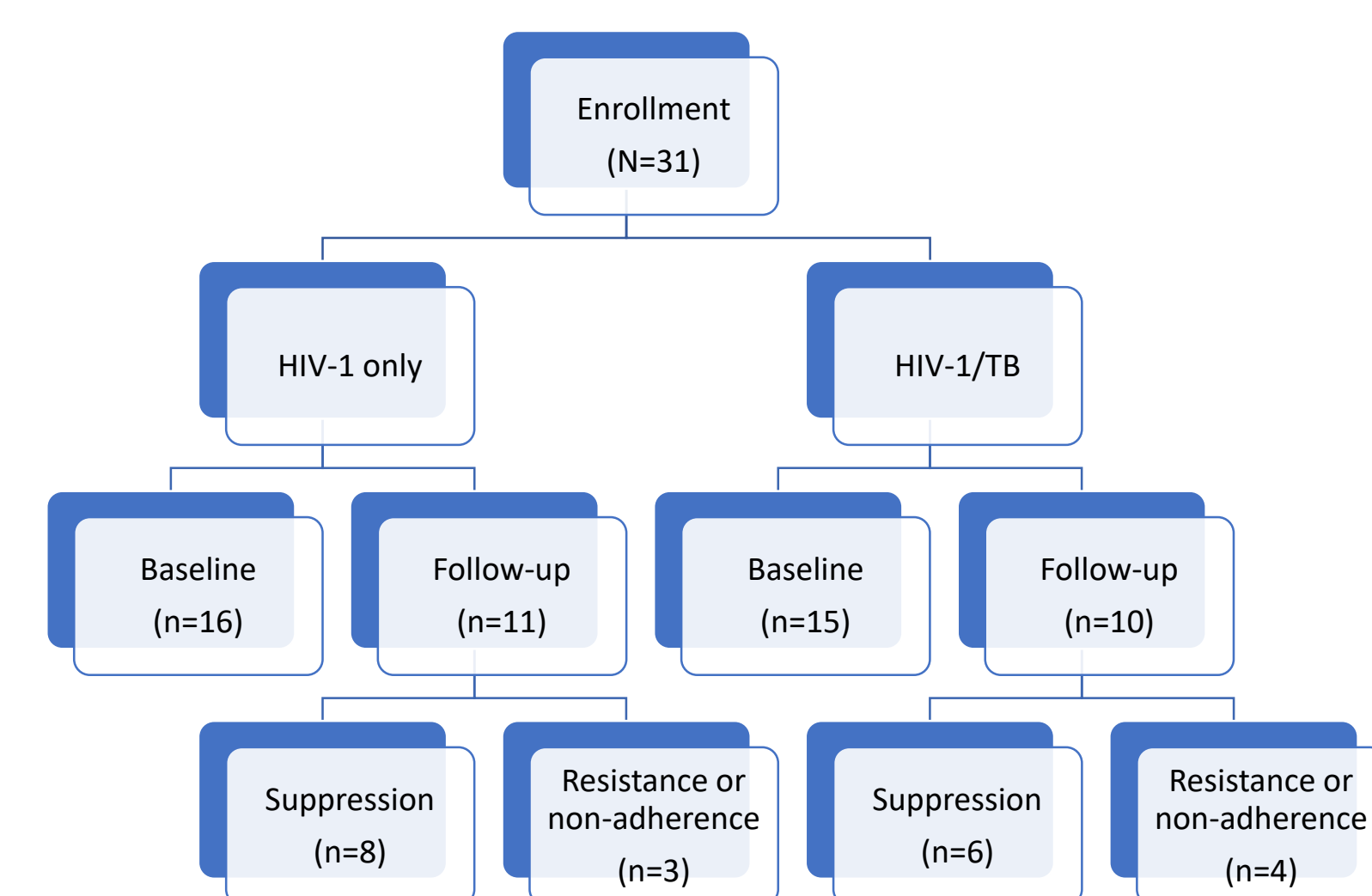

	HIV+ and TB n = 15	HIV+ n = 16	p-value
Age (years)	35 (19 – 48)	34.5 (21 – 56)	0.80
# male (%)	9 (60%)	10 (59%)	0.94
BMI	19.5 (15.4 – 28.5)	20.4 (15.2 – 32.3)	0.33
Log$_{10}$ plasma virus (copies/ml)	5.5 (3.8 – 6.6)	5.6 (3.8 – 6.6)	0.33
CD4+ T cells (cells/mm^3)	141 (12 – 733)	95 (3 – 358)	0.40
CD4:CD8 ratio	0.22 (0.04 – 0.91)	0.11 (0.02 - 0.46)	0.20

1. HIV-1 individuals with active TB as compared to without active TB had a broader and more potent HIV-1 specific neutralizing capacity.
2. The observed HIV-1 specific breadth and potency score is sustained for more than 6 months after treatments.
3. Observed *neutralizing capacity* of treatment-naïve participants either with or without active TB associates significantly with the absolute IgG concentration.

RESULTS

HIV-1/TB and HIV-1 only infected individuals had similar baseline plasma virus levels (p= 0.33) and CD4 counts (p= 0.40). HIV-1/TB individuals had a significantly higher BP score (0.59 ± 0.05, range 0.34-0.98) than the HIV-1 only group (0.43 ± 0.02, range 0.25-0.59, p= 0.006). Four of the HIV-1/TB but none of the HIV-1 only infected individuals had a similar or higher BP score as that observed among 2nd generation bnAbs (BP score range 0.71-0.98, p= 0.04). Neutralization BP score correlated with the total plasma IgG (r = 0.51, p= 0.003), but not with baseline viral load, absolute CD4 count, IL-6, soluble CD163 or MCP-1 concentrations. After completing TB treatment and starting HIV-1 therapy, HIV-1/TB (0.68 ± 0.07, n= 6, range 0.28-0.88) as compared to HIV-1 only infected subjects (0.57 ± 0.07, n= 8, range 0.34-0.82) still had higher neutralizing capacity, but the difference was not statistically significant (p= 0.56). The plasma activity of the 4 HIV-1/TB individuals with high baseline BP score clustered with CD4 binding site and membrane-proximal external region targeting bnAbs.
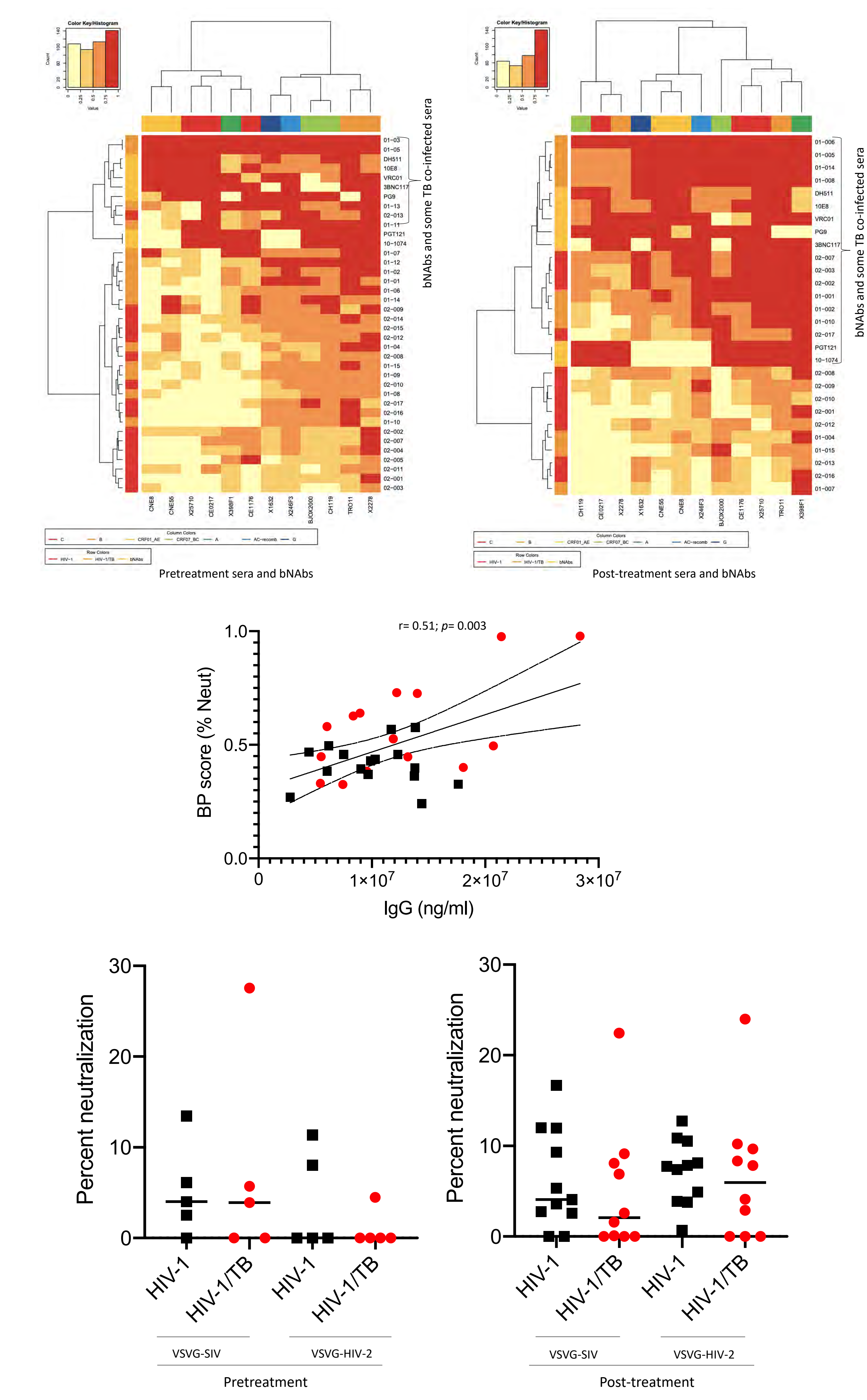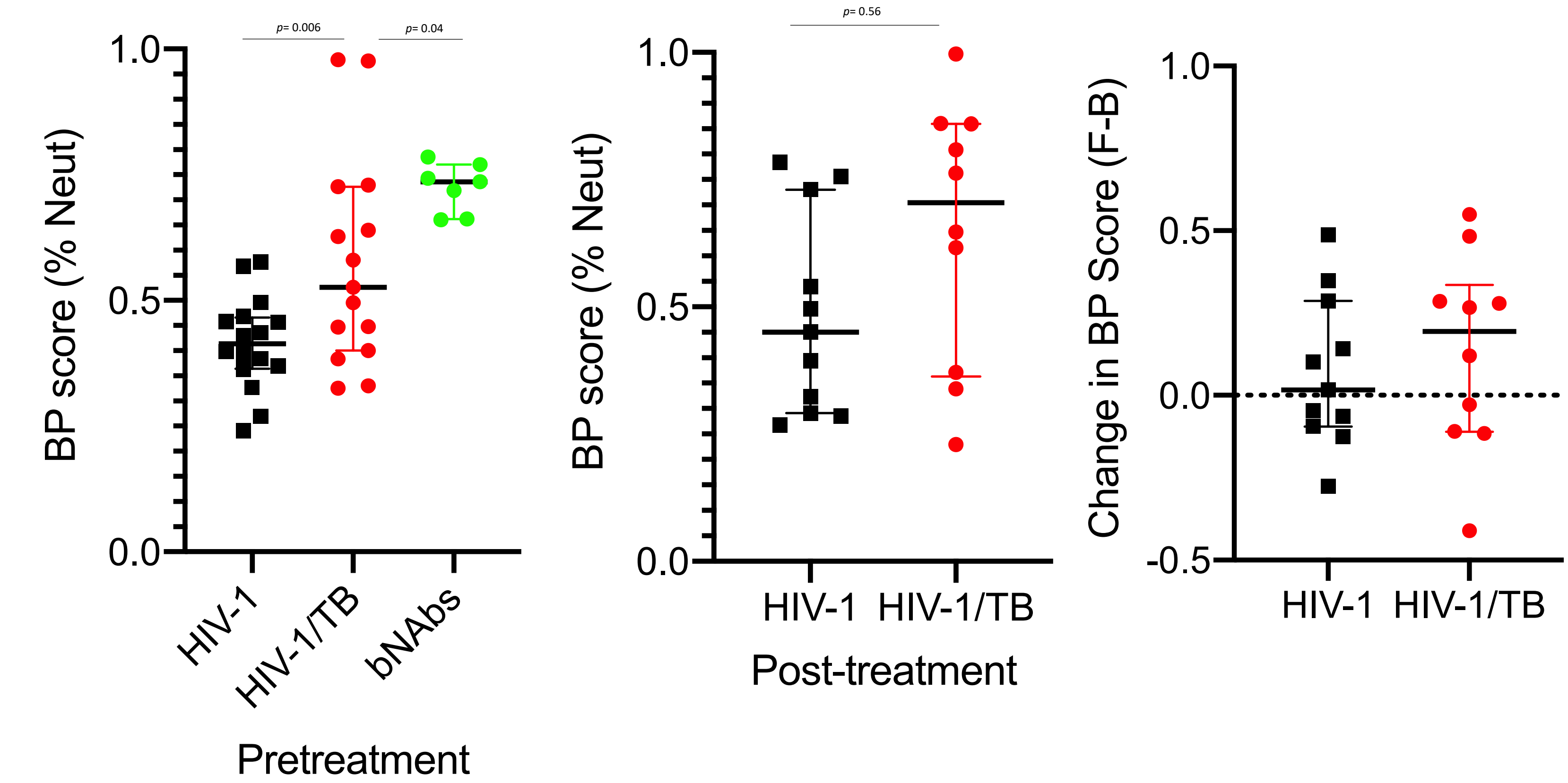
CONCLUSIONS

Our results suggest that active TB enhances anti-HIV-1 antibody response, possibly leading to the emergence of bnAbs that target conserved envelope domains. Dissecting mechanisms that account for the enhanced HIV-1 neutralization in HIV-1 cases with TB could be leveraged in the generation of a more effective humoral response in HIV-1 vaccination and treatment.