

## Expanded View Figures

### Figure EV1. Controls with heat-inactivated sera and dose–response analysis of a panel of anti-HIV-1 Env antibodies.

- A, B Raji-Env cells were incubated 24 h with the indicated antibody and HIHS. After 1 h, C3 surface levels were analyzed by flow cytometry (A). For each antibody, a normalized MFI is calculated by subtracting the MFI of the “no antibody” condition. (nd. not done;  $n = 3$  donors of serum). After 24 h, cell death was determined by flow cytometry (B). The % of CDC was calculated as the relative percentage of dead cells compared to the “no antibody” condition ( $n = 3$  donors of serum).
- C Green: Raji-Env cells were cultured for 24 h with the indicated concentration of each antibody and NHS ( $n = 6$ ). The % of CDC was calculated as the relative percentage of dead cells compared to the “no antibody” condition. Purple: Raji-Env cells were incubated with the indicated concentration of each antibody, and the antibody surface levels were determined by flow cytometry. Results are expressed as the % of cells bound by the antibody.

Data information: Error bars indicate SEM.

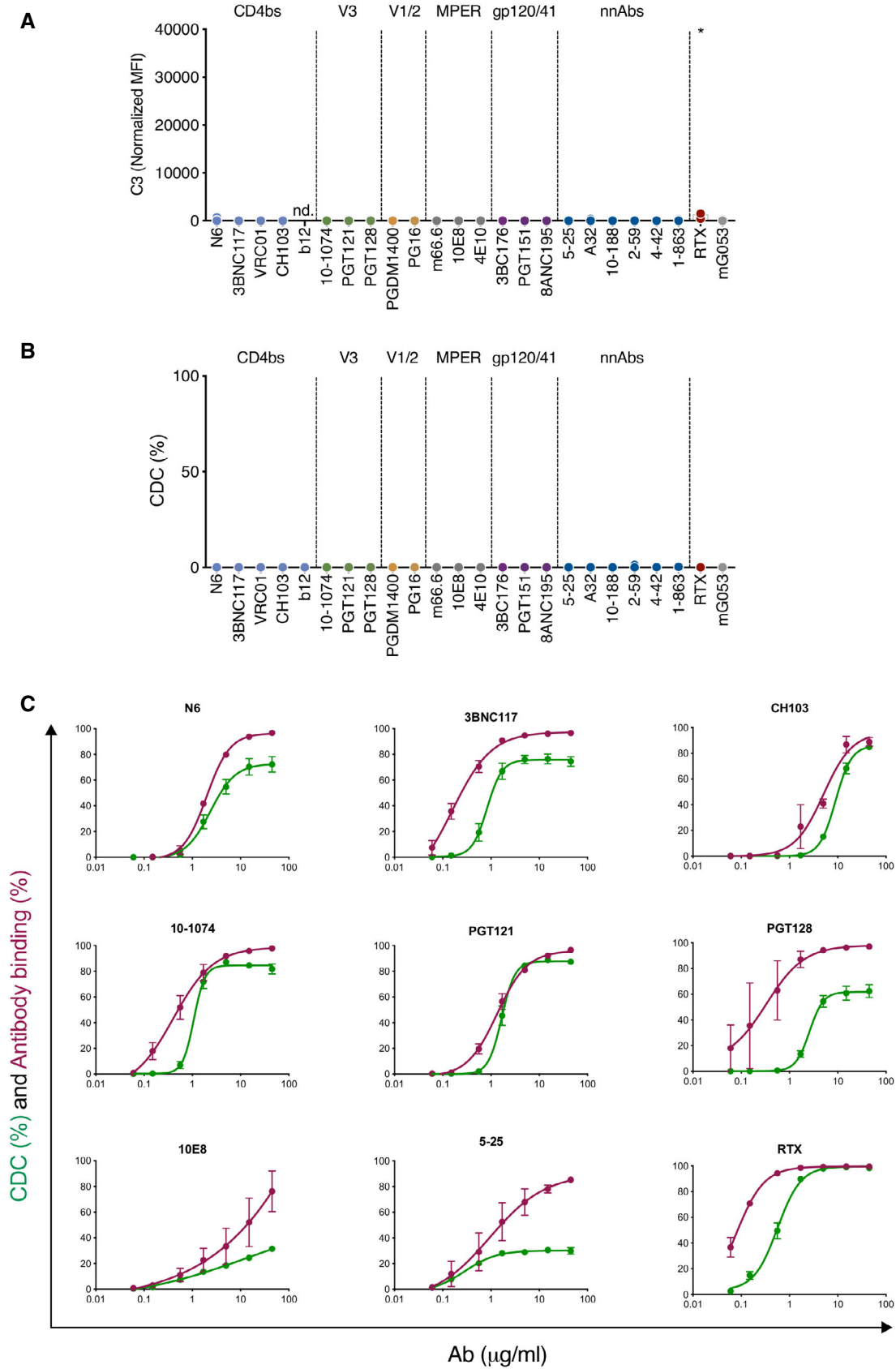
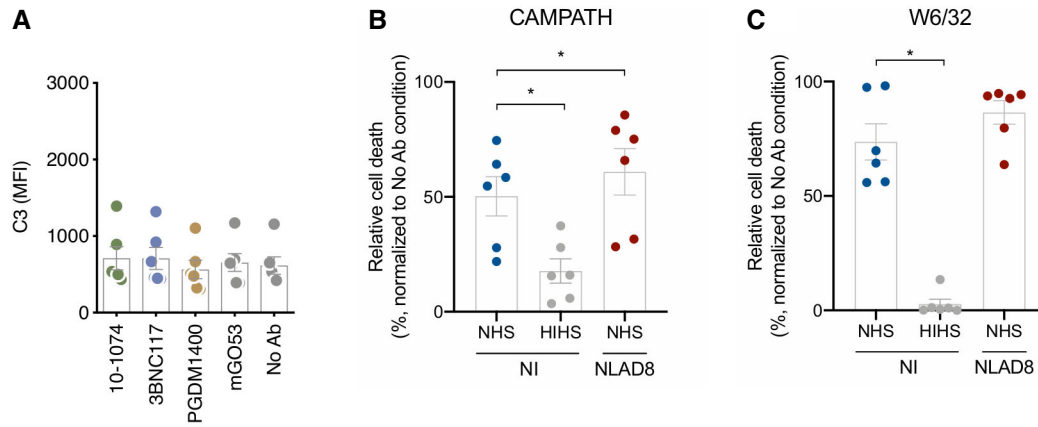


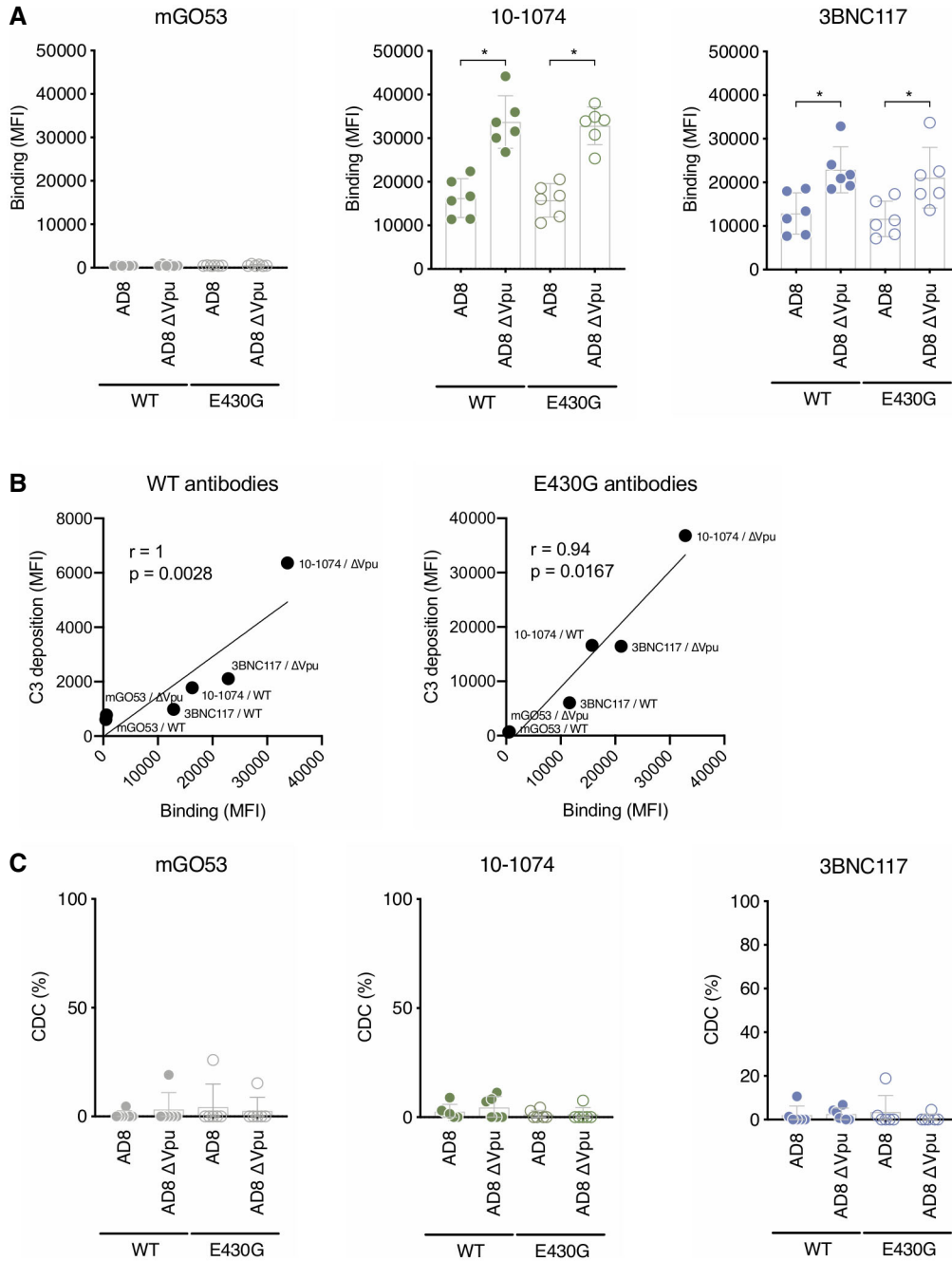
Figure EV1.



**Figure EV2. Primary CD4 T cells are sensitive to CDC triggered by antibodies targeting cellular proteins.**

- A HIV-1-infected (strain NLAD8) CD4 T cells were cultured with the indicated antibody and NHS. After 24 h, the surface levels of C3 on non-infected bystander cells (Gag<sup>-</sup>) were determined by flow cytometry. Results are expressed as MFI of staining. Each dot represents a single donor of CD4 T cells/NHS combination. *n* = 3 donors of CD4 T cells.
- B, C Non-infected or HIV-1-infected (strain NLAD8) CD4 T cells were cultured with W6/32 (anti-HLA-A) or CAMPATH (anti-CD52) and NHS or HIHS for 24 h. The % of CDC was calculated as the relative percentage of dead cells compared to the “no antibody” condition. Each dot represents a single donor of CD4 T cells. *n* = 6 donors of CD4 T cells.

Data information: Error bars indicate SEM. \**P* < 0.05, Wilcoxon test; only significant comparisons are depicted.



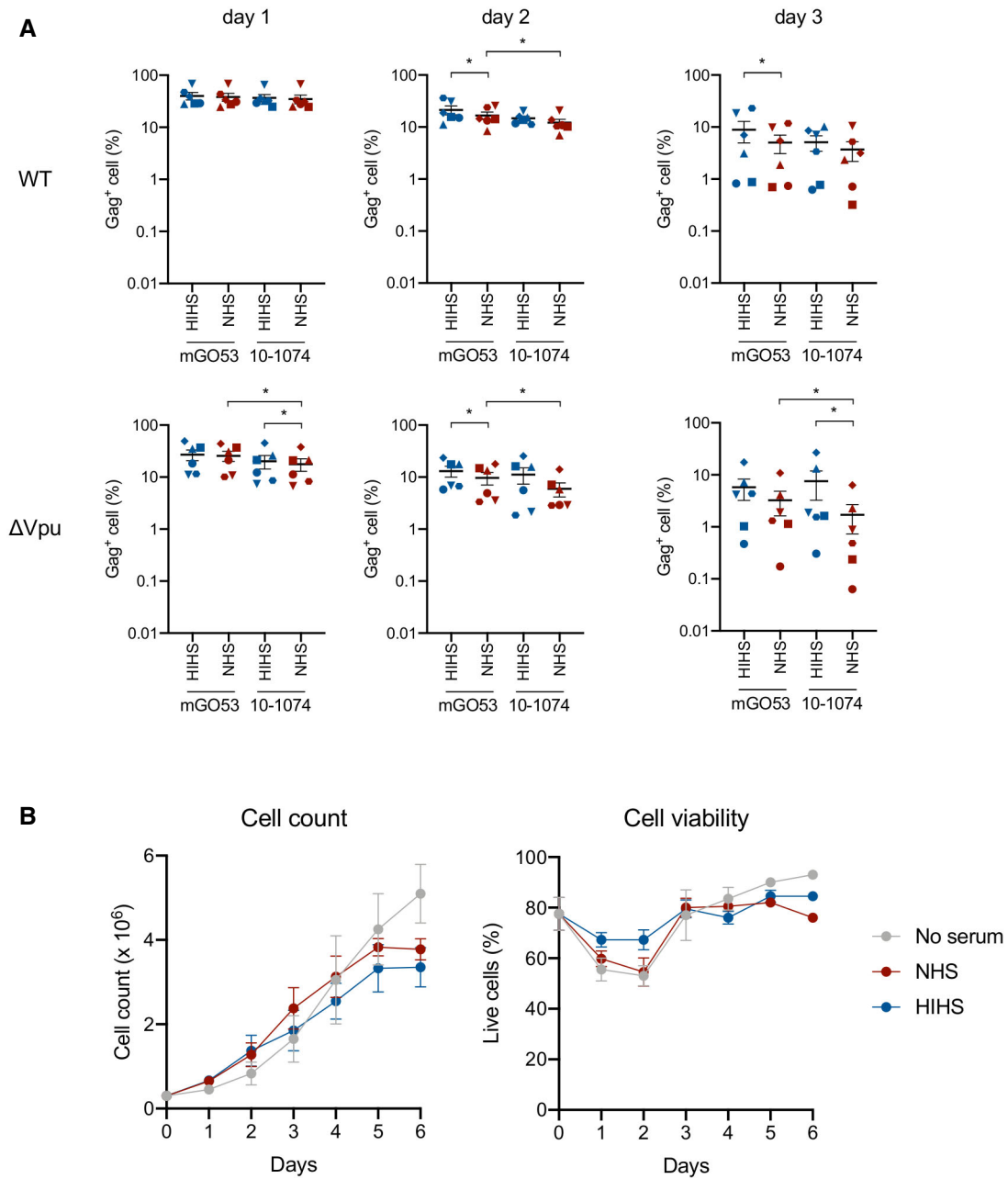
**Figure EV3. Antibody binding correlates to complement deposition.**

A Primary CD4 T cells were infected by HIV-1 (strain NLAD8 WT or ΔVpu). The binding of the WT or E430G indicated antibodies was measured by flow cytometry. Results are expressed as median fluorescence (MFI) of staining on infected (Gag<sup>+</sup>) cells. Each dot represents a single donor of CD4 T cells. *n* = 6 donors of CD4 T cells.

B Correlations between WT (left) or E430G (right) antibody binding and C3 deposition on CD4 T cells infected with WT or ΔVpu HIV-1 (strain NLAD8). Each dot is the mean of 6 donors of CD4 T cells. Correlation was analyzed by Spearman correlation. Correlation coefficient (*r*) and *P*-value are indicated.

C WT or ΔVpu HIV-1-infected CD4 T cells (strain NLAD8) were cultured with the indicated WT or E430G mutant antibodies and NHS or HIHS to determine complement-mediated cytotoxicity. After 24 h, the percentage of infected (Gag<sup>+</sup>) cells in each condition was determined by flow cytometry. For each antibody, the % of CDC was calculated at 24 h as the % of disappearance of Gag<sup>+</sup> cells in NHS compared to HIHS. Each dot represents a single donor of CD4 T cells. *n* = 6 donors of CD4 T cells.

Data information: Error bars indicate SEM. \**P* < 0.05, Wilcoxon test; only significant comparisons are depicted.



**Figure EV4. 10-1074<sup>E430G</sup> does not trigger CDC of infected cells.**

A Frequency of live HIV-1-infected cells (NLAD8 WT or ΔVpu strain) at days 1, 2, and 3 after incubation with the indicated antibodies (E430G), and with NHS or HIHS. Each donor of CD4 T cells is represented by a different symbol. *n* = 6 donors of CD4 T cells. Error bars indicate SEM. \**P* < 0.05, Wilcoxon test; only significant comparisons are depicted.

B Non-infected primary CD4 T cells were incubated or not with 50% NHS or HIHS, and cell count and viability were measured each day for 6 days (*n* = 4). Error bars indicate SEM.