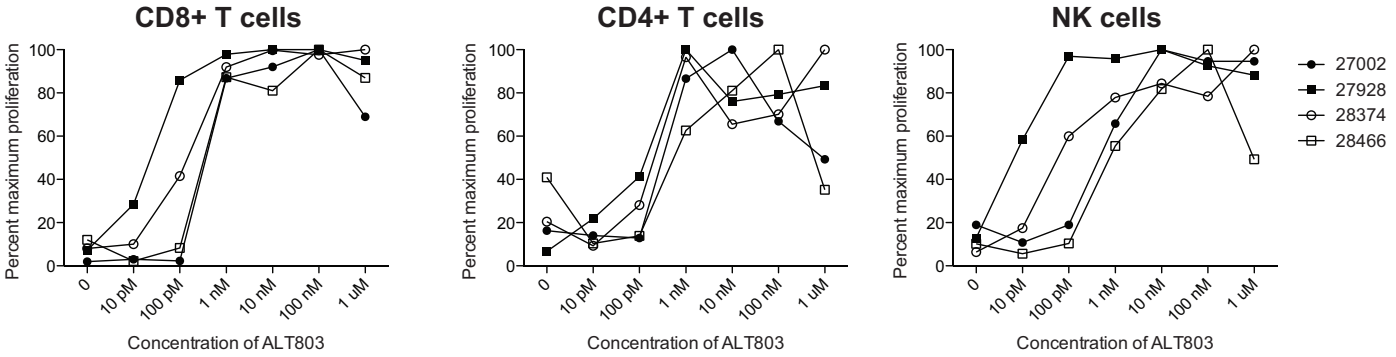
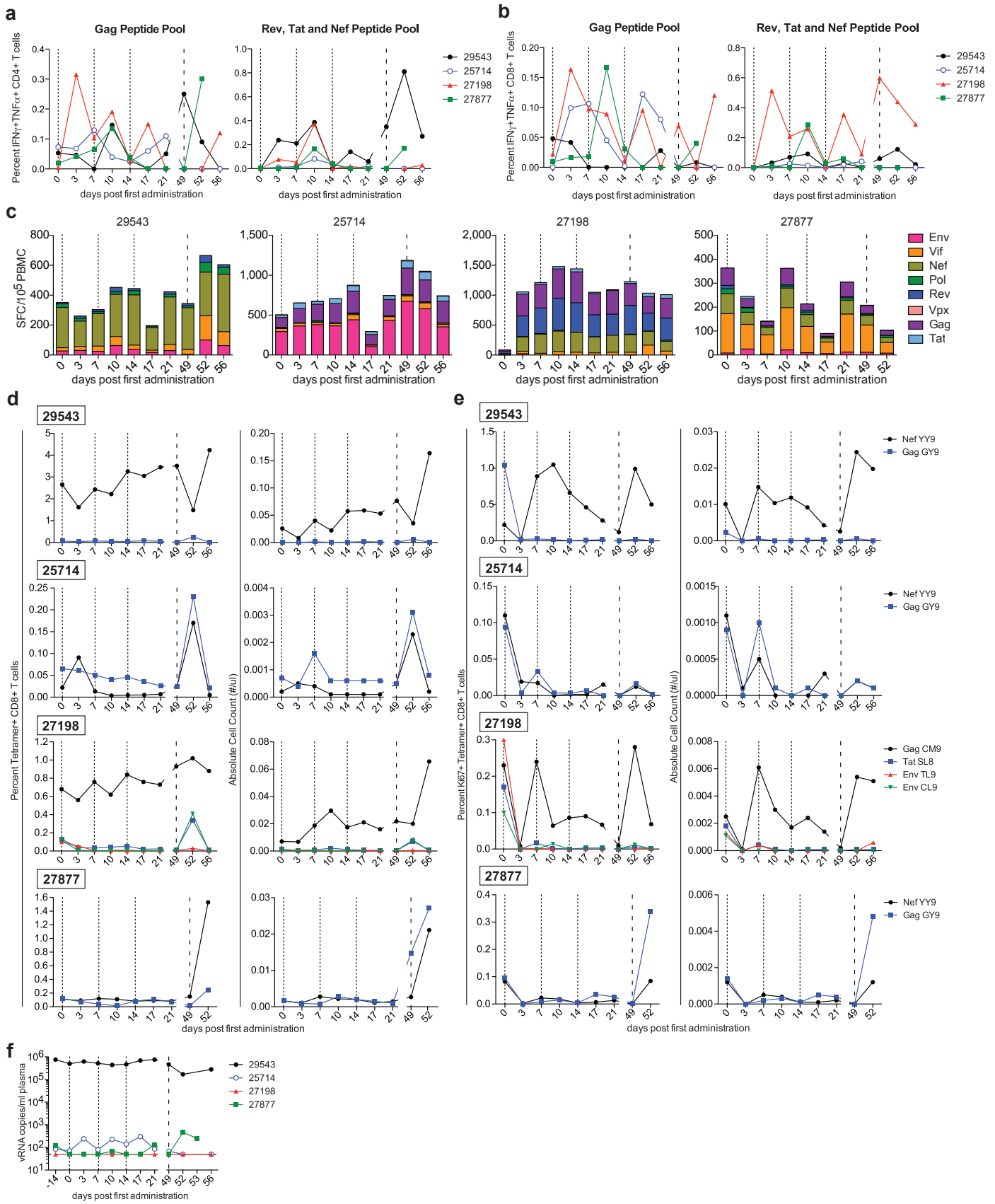
Supplementary Table 1. Animals used for *in vivo* studies

Animal ID	SIV status	Figures Referenced
27001	Uninfected	Fig. 1
28390	Uninfected	Fig. 1
24802	Uninfected	Fig. 1
29105	Uninfected	Fig. 1
29543	SIV-infected (progressor)	Fig. 2, Supp. Fig. 2, Supp. Fig. 3
25714	SIV-infected (controller)	Fig. 2, Supp. Fig. 2, Supp. Fig. 3, Supp. Fig. 4
27198	SIV-infected (controller)	Fig. 2, Fig. 3, Fig. 4, Supp. Fig. 2, Supp. Fig. 3, Supp. Fig. 4, Supp. Fig. 5, Supp. Fig 6,
27877	SIV-infected (controller)	Fig. 2, Supp. Fig. 2, Supp. Fig. 3
26923	SIV-infected (controller)	Fig. 3, Fig. 4, Supp. Fig. 3, Supp. Fig. 4, Supp. Fig. 5, Supp. Fig 6, Supp. Fig. 7
25884	SIV-infected (controller)	Fig. 3, Fig. 4, Supp. Fig. 3, Supp. Fig. 4, Supp. Fig. 5, Supp. Fig 6, Supp. Fig. 7
31210	SIV-infected (progressor)	Fig. 3, Fig. 4
31252	SIV-infected (progressor)	Fig. 3, Fig. 4
31511	SIV-infected (progressor)	Fig. 3, Fig. 4

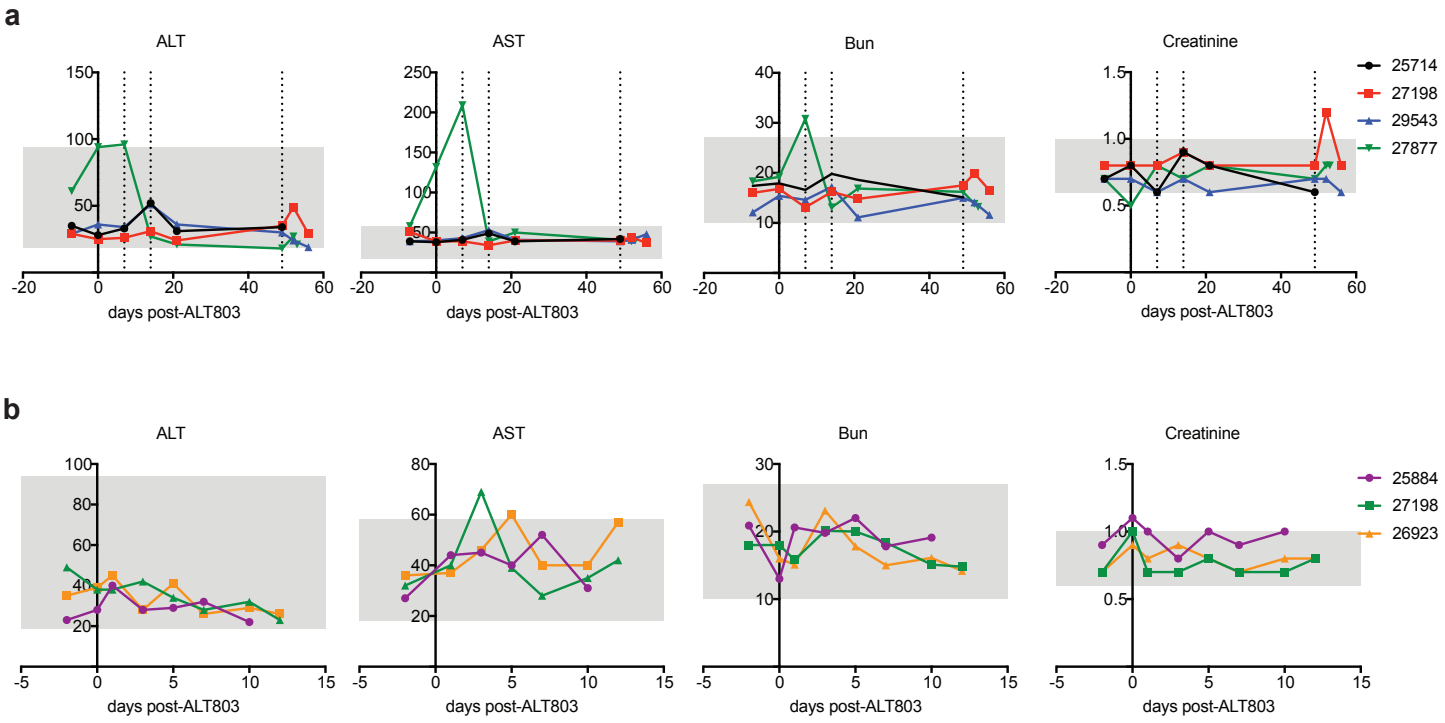


Supplementary Figure 1. ALT-803 induces proliferation of rhesus macaque T cells and NK cells *in vitro*. PBMC from SIV-naïve rhesus macaque (n=4) were CFSE-labeled and cultured for 7 days in media with the indicated amounts of ALT-803. Cells were analyzed by flow cytometry to determine cell proliferation. Proliferation of $CD8^+$ T cells, $CD4^+$ T cells, and NK cells determined by the percent of $CFSE^{dim}$ cells as a percentage of maximum proliferation.

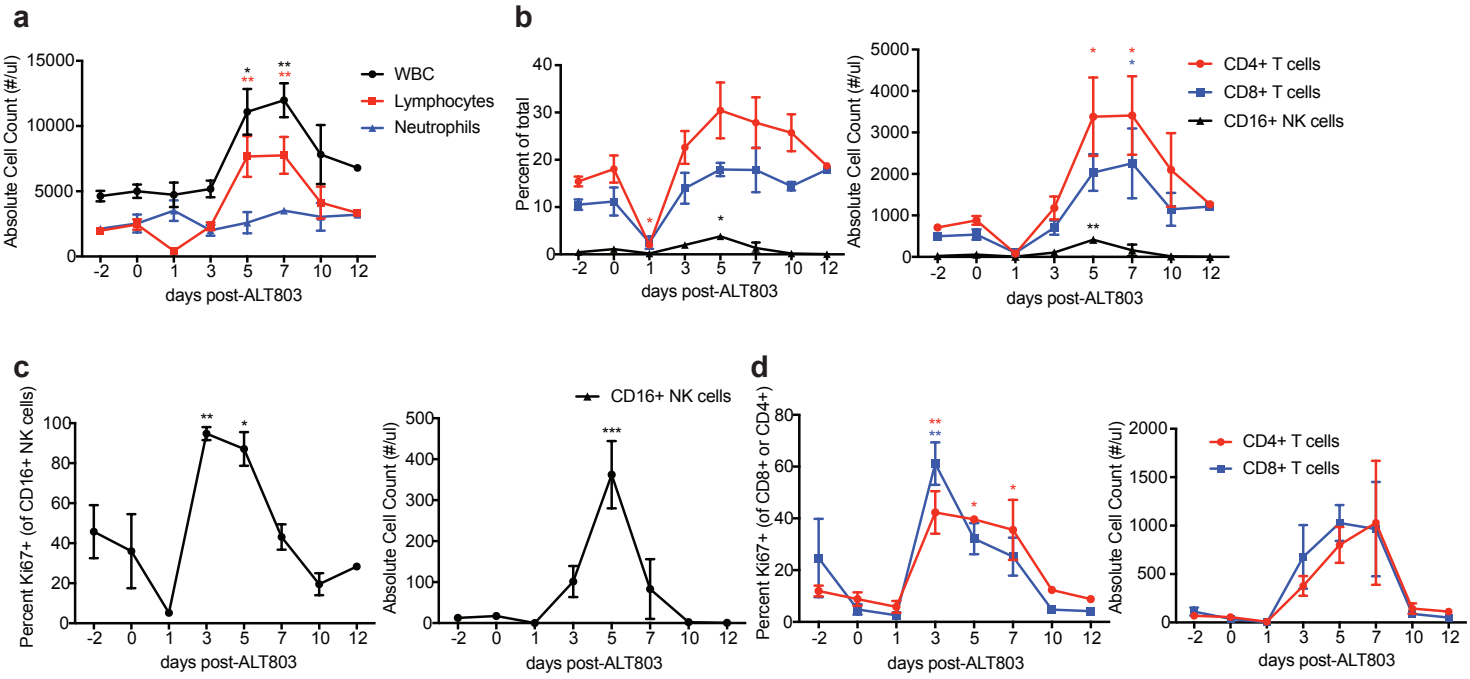


Supplementary Figure 2. SIV-specific T cell immunity in SIV-infected animals after administration of ALT-803. SIV-infected rhesus macaques (n=4) were injected intravenously with 6 ug/kg ALT-803 at days 0, 7 and 14 (indicated by thin dashed lines) and subsequently with 100 ug/kg

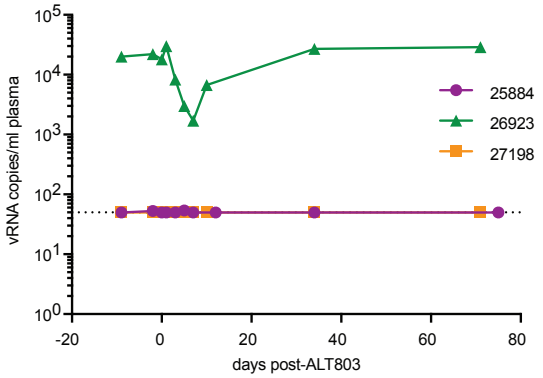
ALT-803 at day 49 (indicated by a thick dashed line). Gag-specific and Rev, Tat and Nef-specific **(a)** $CD4^+$ and **(b)** $CD8^+$ T cell responses were measured by ICS. Results are background subtracted. **(c)** IFN-γ ELISPOT responses to the entire SIV proteome were measured over time. **(d)** Frequency and absolute count of tetramer-positive $CD8^+$ T cells post ALT-803. **(e)** Frequency and absolute count of proliferating tetramer-positive $CD8^+$ T cells as measured by Ki67 post ALT-803. **(f)** SIV viral loads from 4 macaques during ALT-803 treatment. Limit of detection (50 vRNA copies/ml plasma) is denoted by black dotted line. Animal 27877 was euthanized at day 53 post ALT-803 due to complications from an unrelated Shigella infection acquired from a cagemate.



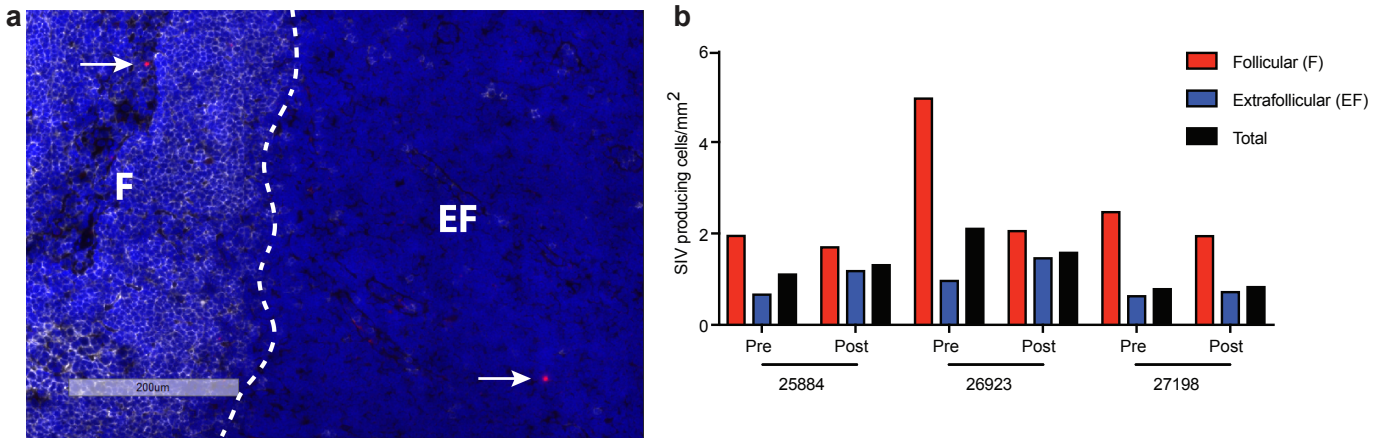
Supplementary Figure 3. ALT-803 has no adverse effect on liver or kidney function in rhesus macaques. (a,b) Serum chemistry analysis of RM receiving ALT-803 intravenously. Gray boxes represent the expected ranges of alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (Bun), and creatinine serum concentrations based on RM population statistics at the Oregon National Primate Research Center. **(a)** SIV-infected rhesus macaques (n=4) were injected intravenously with 6 ug/kg ALT-803 at days 0, 7 and 14 and subsequently with 100 ug/kg ALT-803 at day 49 (indicated by dashed lines). **(b)** SIV-infected controller rhesus macaques (n=3) were administered 100 ug/kg of ALT-803 intravenously at day 0.



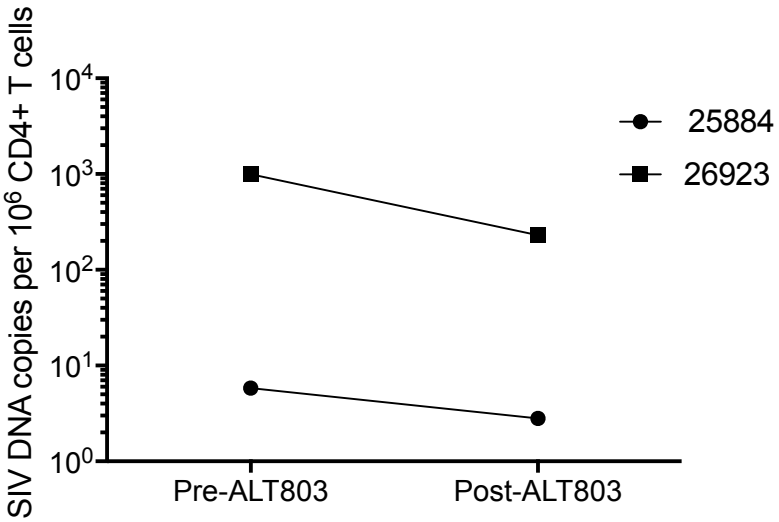
Supplementary Figure 4. *In vivo* administration of ALT-803 in controller SIV-infected rhesus macaques. SIV-infected controller rhesus macaques (n=3) were administered 100 ug/kg of ALT-803 intravenously. **(a)** White blood cells (WBC), lymphocytes, and neutrophils as well as **(b)** $CD4^+$ T cell, $CD8^+$ T cells, and $CD16^+$ NK cells were analyzed from whole blood. Proliferation of **(c)** $CD16^+$ NK cells, **(d)** $CD4^+$ and $CD8^+$ T cells were determined as a percentage of $Ki67^+$ cells of that particular lymphocyte population. Absolute counts were calculated based on the percentage of the particular cell subset and the WBC count. Data shown are means (± SEM) of combined data from all four animals. *, P<0.05; **, P<0.01; ***, P<0.001 comparing time points to time point zero.



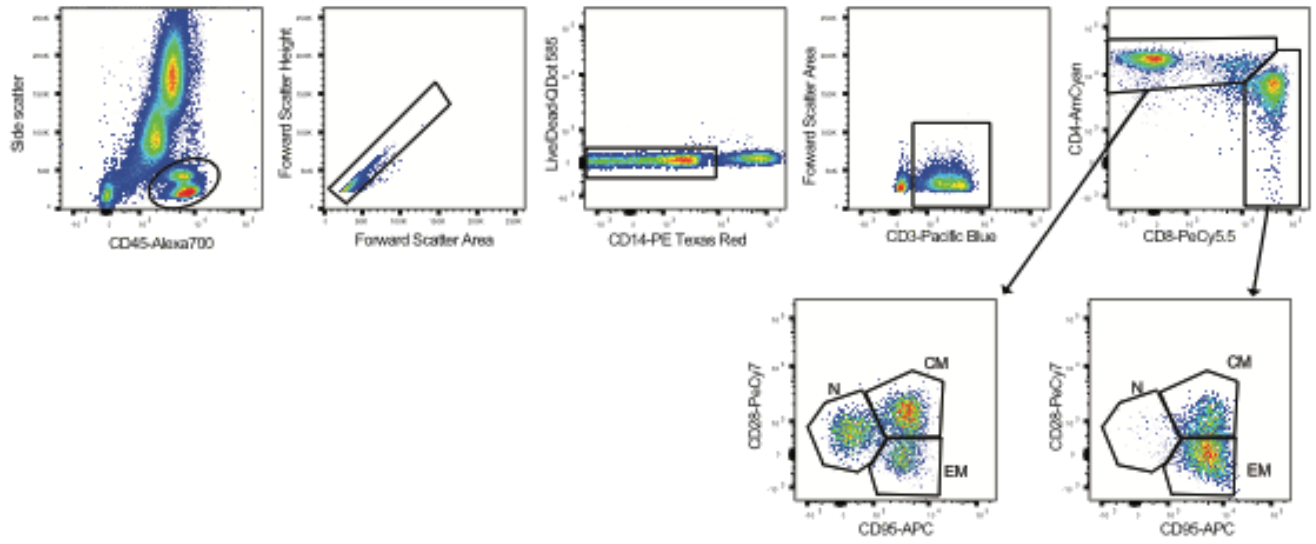
Supplementary Figure 5. Plasma viral loads in SIV-infected rhesus macaques following ALT-803 administration. Plasma viral loads of SIV-infected rhesus macaques (n=3) are shown during the period of 100 ug/kg ALT-803 administered intravenously. Limit of detection (50 vRNA copies/ml plasma) is denoted by black dotted line.



Supplementary Figure 6. ALT-803 reduces the number of SIV-producing cells within B cell follicles. SIV-infected controller rhesus macaques (n=3) were administered 100 ug/kg of ALT-803 intravenously. Lymph nodes were sampled before ALT-803 treatment and 5 days post-treatment and RNAscope analysis was used to determine the number of SIV-producing cells in lymph nodes. **(a)** Representative image of RNAscope analysis of lymph node. RNA+ cells (red, white arrows) detected by RNAscope® methodology in lymph node tissue section of SIVmac239-infected rhesus macaque prior to treatment with ALT803 (animal 25884). B cell follicle (demarcated by white line) was determined morphologically by staining with CD20 (white). Tissue was counterstained with DAPI (blue) to identify cell nuclei. Bar indicates 200 µm. **(b)** Compiled data of the number of SIV-producing cells in B cell follicular (F) or extrafollicular (EF) space within lymph nodes of SIV-infected controller macaques pre and post ALT-803 treatment with ALT-803.



Supplementary Figure 7. Levels of cell-associated SIV in purified CD4+ T cells. In SIV-infected controller rhesus macaques with sufficient starting material, lymph node resident CD4+ T cells were isolated via MACS and assayed for cell-associated SIV DNA viral load pre- and 5-days post 100 ug/kg of ALT-803.



Supplementary Figure 8. Example of gating strategy used in flow cytometric analysis.