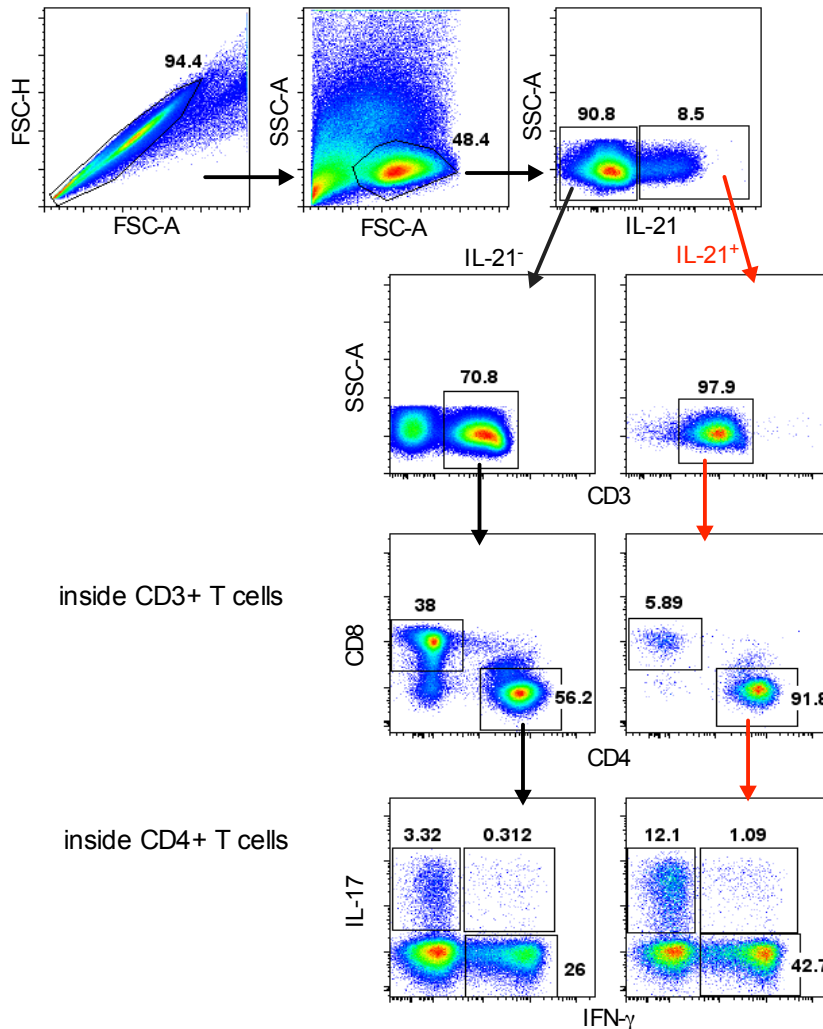


## Supplemental data

### Supporting Figure 1

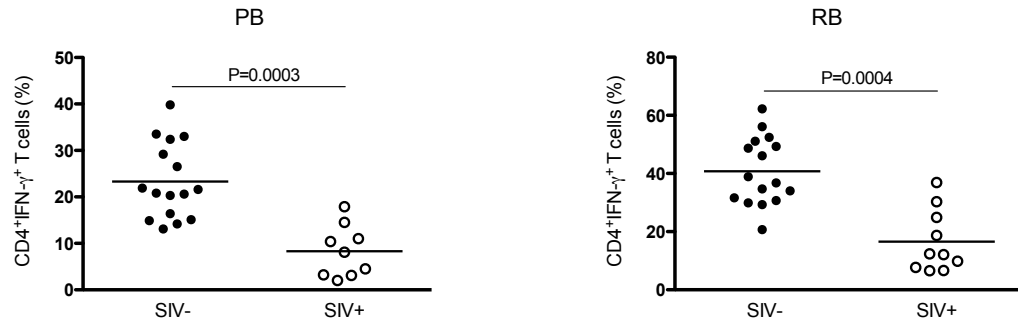


**Figure S1. Phenotype of IL-21-producing cells in SIV-uninfected nonhuman primates.**

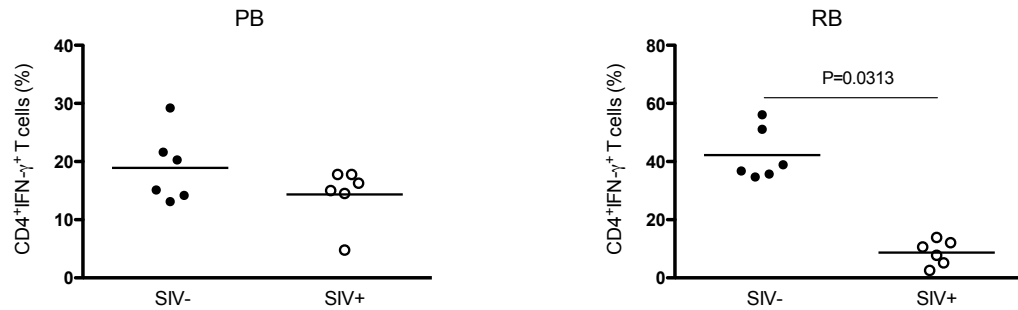
Characterization of IL-21-producing cells in the PB of SIV-uninfected RMs and SMs. Lymphocytes that produce (red arrows) or not (black arrows) IL-21 were compared for the expression of CD3, CD4 and CD8, as well as production of IL-17 and/or IFN- $\gamma$  following stimulation with PMA and Ionomycin.

## Supporting Figure 2

A: i.r. SIV-infection

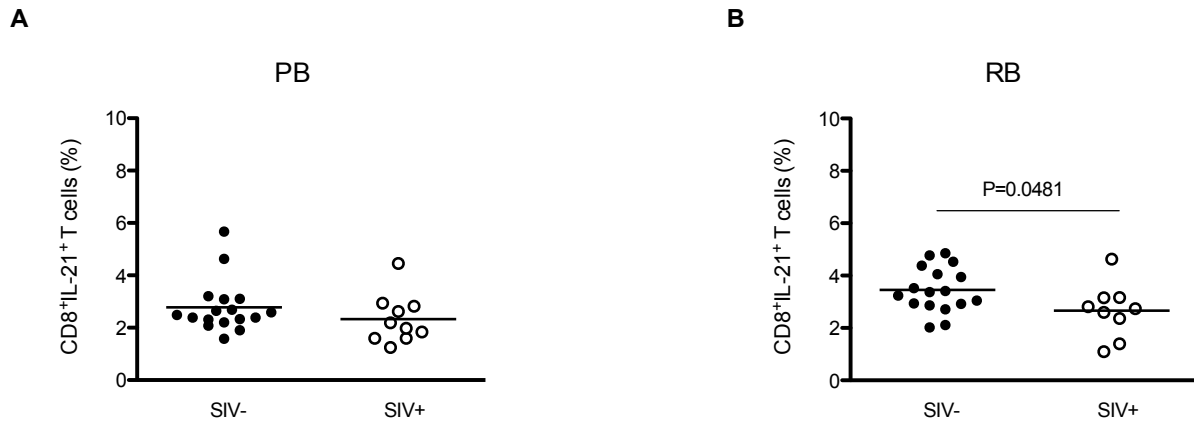


B: i.v. SIV-infection



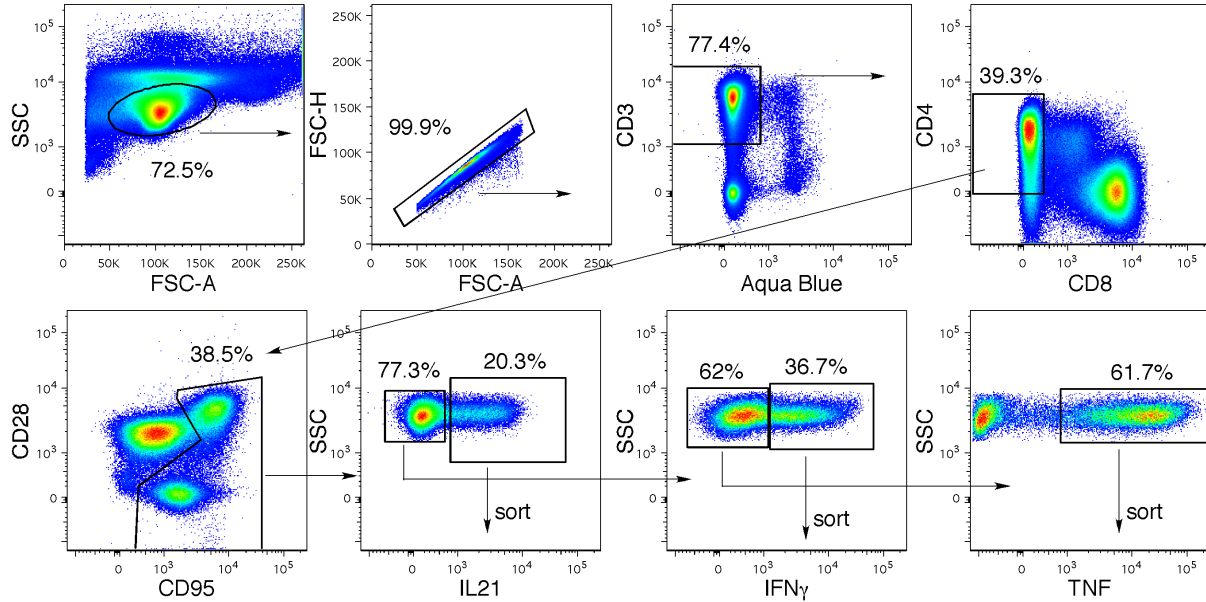
**Figure S2. Levels of blood and intestinal CD4<sup>+</sup>IFN- $\gamma$ <sup>+</sup> T-cells in chronic SIV infection of RMs.** The percentages of circulating (left panels) and intestinal (right panels) CD4<sup>+</sup>IFN- $\gamma$ <sup>+</sup> T-cells were compared between chronically, intra-rectal (A) or intra-venous (B) SIV-infected (open circle) and uninfected (full circle) RMs. Statistical analyses were performed to compare the levels of CD4<sup>+</sup>IFN- $\gamma$ <sup>+</sup> T-cells between SIV-infected and uninfected animals.

### Supporting Figure 3



**Figure S3. Levels of blood and intestinal CD8<sup>+</sup>IL-21<sup>+</sup> T-cells in chronic intra-rectal SIV infection of RMs.** The percentages of circulating (A) and intestinal (B) CD8<sup>+</sup>IL-21<sup>+</sup> T-cells were compared between chronically, i.r. SIV-infected (open circle) and uninfected (full circle) RMs. Statistical analyses were performed to compare the levels of CD8<sup>+</sup>IL-21<sup>+</sup> T-cells between SIV-infected and uninfected animals.

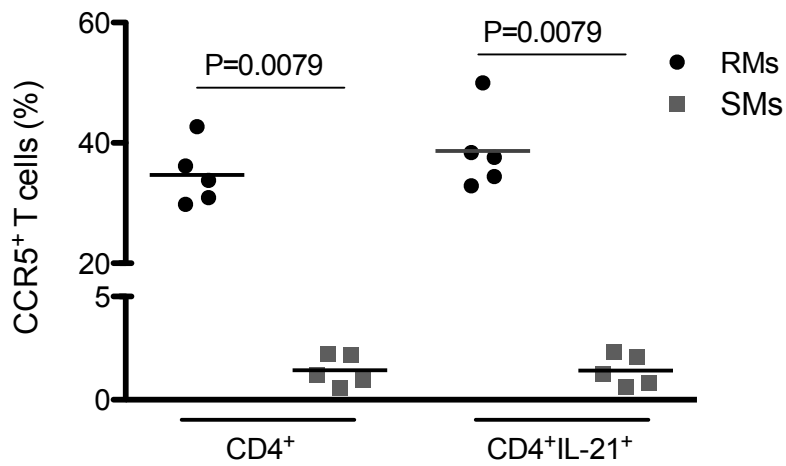
## Supporting Figure 4



### Figure S4. Sorting of splenic cytokine-producing CD4<sup>+</sup> T-cells in SIV-infected RMs.

Representative flow plots showing the strategy used to sort CD4<sup>+</sup>IL-21<sup>+</sup>, CD4<sup>+</sup>IFN- $\gamma$ <sup>+</sup>, and CD4<sup>+</sup>TNF- $\alpha$ <sup>+</sup> T-cells from the spleen of 4 SIV-infected RMs. Cells were initially gated based on light scatter, followed by positive staining for CD3 without binding to the dead cell dye, and then for CD4 (without CD8 staining). Memory CD4<sup>+</sup> T-cells, gated based upon characteristic expression patterns of CD28 and CD95, were then divided based on the production of IL-21, TNF- $\alpha$ , or IFN- $\gamma$ . The infection frequencies of the purified populations were then determined by qPCR for SIVgag DNA.

### Supporting Figure 5



**Figure S5. Levels of CCR5 expression on intestinal CD4<sup>+</sup>IL-21<sup>+</sup> T-cells from natural and nonnatural hosts for SIV.** Percentages of intestinal CD4<sup>+</sup> and CD4<sup>+</sup>IL-21<sup>+</sup> T-cells that express CCR5 in healthy, SIV-uninfected RMs (black circle) and SMs (gray square). Statistical analyses were performed to compare the levels of CCR5<sup>+</sup> T-cells between RMs and SMs.