

Supplementary Figure 1. Human CD11c+ dendritic cells are present throughout the female reproductive tract of BLT mice. Immunohistochemical analysis of the entire FRT of a HIV negative BLT mouse demonstrates the presence of CD11c+ cells in the vagina, cervix and uterus (CD11c positive cells are stained brown) (scale bars indicate $100 \mu \mathrm{~m})$.


Supplementary Figure 2. Human CD68+ macrophages are present throughout the female reproductive tract of BLT mice. Immunohistochemical analysis of the entire FRT of a HIV-negative BLT mouse demonstrates the presence of CD68+ cells in the vagina, cervix and uterus (CD68 positive cells are stained brown) (scale bars indicate $100 \mu \mathrm{~m}$ ). It should be noted that CD68 has conventionally been regarded as a macrophage marker $(24,72)$ and in this study, we have utilized CD68 as a marker for human macrophages present in the FRT. However, a subset of immature dendritic cells in PB and myeloid dendritic cells in the kidney have been shown to express CD68 and it is important to note that a small proportion of the CD68 expressing cells that we detected could be dendritic cells (72-76).


Human

Supplementary Figure 3. Comparable proportions of memory CD4 ${ }^{+}$T cells in PB from humans and BLT mice express $\alpha 4 \beta 7$. Flow cytometric analyses of $\alpha 4 \beta 7$ expression on memory CD4 ${ }^{+}$T cells of PB from humans (black dots, $\mathrm{n}=4$ ) and PB (grey dots, $\mathrm{n}=18$ ), FRT (grey diagonal stripes, $\mathrm{n}=5$ ) and CVS (grey solid color, $n=13$ ) from HIV negative BLT mice. A Mann-Whitney test with a Bonferroni step-down (Holm) correction was used to compare the percentages of memory CD4 ${ }^{+}$T cell expressing $\alpha 4 \beta 7$ in the PB of humans and PB, FRT and CVS of BLT mice ( ${ }^{*} p<0.05,{ }^{* *} p<0.01,{ }^{* * *} p<0.001,{ }^{* * * *} p<0.0001$ ). There was no significant difference in the percentage of memory CD4+ T cells expressing $\alpha 4 \beta 7$ in PB between humans and BLT mice ( $p=0.13$ ). Further, the proportion of memory CD4 ${ }^{+}$T cell expressing $\alpha 4 \beta 7$ in the FRT and CVS in BLT mice were significantly lower than in the PB (PB vs. FRT $p=0.003$, PB vs. CVS p<0.0001), whereas there was no difference between the FRT and CVS $(p=0.13)$. Bars represent mean values $( \pm$ SEM $)$.

## Supplementary table 1. Exposure route and inoculum used for HIV infected BLT mice

| Figure | Total ( n ) | Exposure route and inoculum |
| :---: | :---: | :---: |
| 3A | 1 | Vaginal: Cell-free HIVJR-CSF |
| 3B | 21 | Vaginal: Cell-free HIVJR-CSF ( $n=7$ ) <br> Vaginal: Cell-associated HIVJR-CsF ( $\mathrm{n}=12$ ) <br> Vaginal: Cell-free HIV RHPA $^{(n=2)}$ |
| 3 C | 16 | Rectal: Cell-free HIVJR-CSF ( $\mathrm{n}=16$ ) |
| 3D | 14 | Oral: Cell-free HIVJR-CSF ( $\mathrm{n}=7$ ) <br> Oral: Cell-associated HIVJr-CsF (n=7) |
| 4A | 18 | Vaginal: Cell-free HIVJR-CSF ( $\mathrm{n}=7$ ) <br> Vaginal: Cell-associated HIVJr-CSF ( $n=9$ ) <br> Vaginal: Cell-free HIV ${ }_{\text {RHPA }}(\mathrm{n}=2)$ |
| 4B | 11 | Rectal: Cell-associated HIVJR-CsF ( $\mathrm{n}=11$ ) |
| 4 C | 12 | Oral: Cell-free HIVJR-CSF $(\mathrm{n}=12)$ |
| 4D | 7 | Vaginal: Cell-free HIVJR-CsF ( $\mathrm{n}=4$ ) <br> Rectal: Cell-free HIVJR-CSF ( $\mathrm{n}=2$ ) <br> Oral: Cell-free HIVJR-CsF ( $\mathrm{n}=1$ ) |
| 5A | 18 | Vaginal: Cell-free HIVJR-CSF ( $n=7$ ) <br> Vaginal: Cell-associated HIVJR-CSF $(n=9)$ <br> Vaginal: Cell-free HIV ${ }_{\text {RHPA }}(\mathrm{n}=2)$ |
| 5B | 11 | Rectal: Cell-associated HIVJR-CsF ( $\mathrm{n}=11$ ) |
| 5C | 1 | Oral: Cell-free HIVJR-CsF |
| 6A, B and C | 6 | Vaginal: Cell-associated HIV ${ }_{\text {JR-CSF }}(\mathrm{n}=6)$ |
| 7A, left panel | 8 | Vaginal: Cell-free HIVJR-CsF ( $n=1$ ) <br> Vaginal: Cell-associated HIVJR-CSF $(n=4)$ <br> Rectal: Cell-free HIVJR-CsF ( $\mathrm{n}=2$ ) <br> Oral: Cell-associated HIVJR-CSF $(\mathrm{n}=1)$ |
| 7A, right panel | 5 | Vaginal: Cell-associated HIVJR-CSF ( $\mathrm{n}=4$ ) <br> Oral: Cell-associated HIVJR-CSF $(\mathrm{n}=1)$ |
| 7B | 16 | Vaginal: Cell-free $\operatorname{HIV}_{\text {JR-CsF }}(\mathrm{n}=9)$ <br> Rectal: Cell-free HIVJR-CsF ( $\mathrm{n}=2$ ) <br> Vaginal: Cell-associated HIVJR-CsF $(n=4)$ <br> Oral: Cell-associated HIVJR-CsF $(\mathrm{n}=1)$ |
| 7C | 13 | Vaginal: Cell-free HIVJR-CsF ( $\mathrm{n}=13$ ) |
| 7D | 9 | Vaginal: Cell-free HIVJR-CsF ( $\mathrm{n}=9$ ) |
| 7E | 8 | Vaginal: Cell-associated HIVJR-CSF ( $\mathrm{n}=8$ ) |

