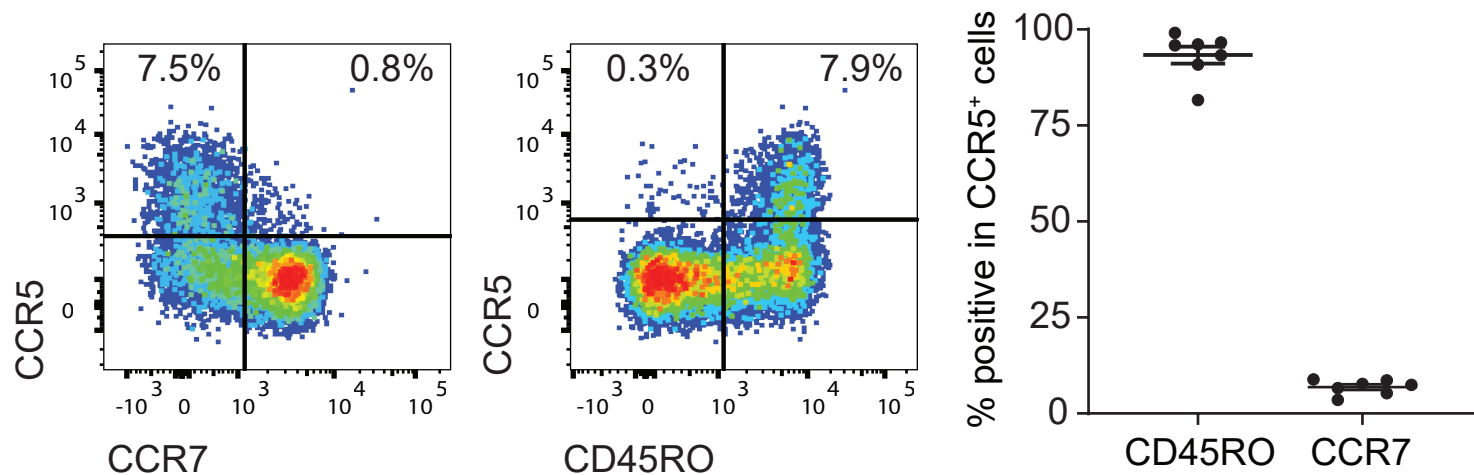
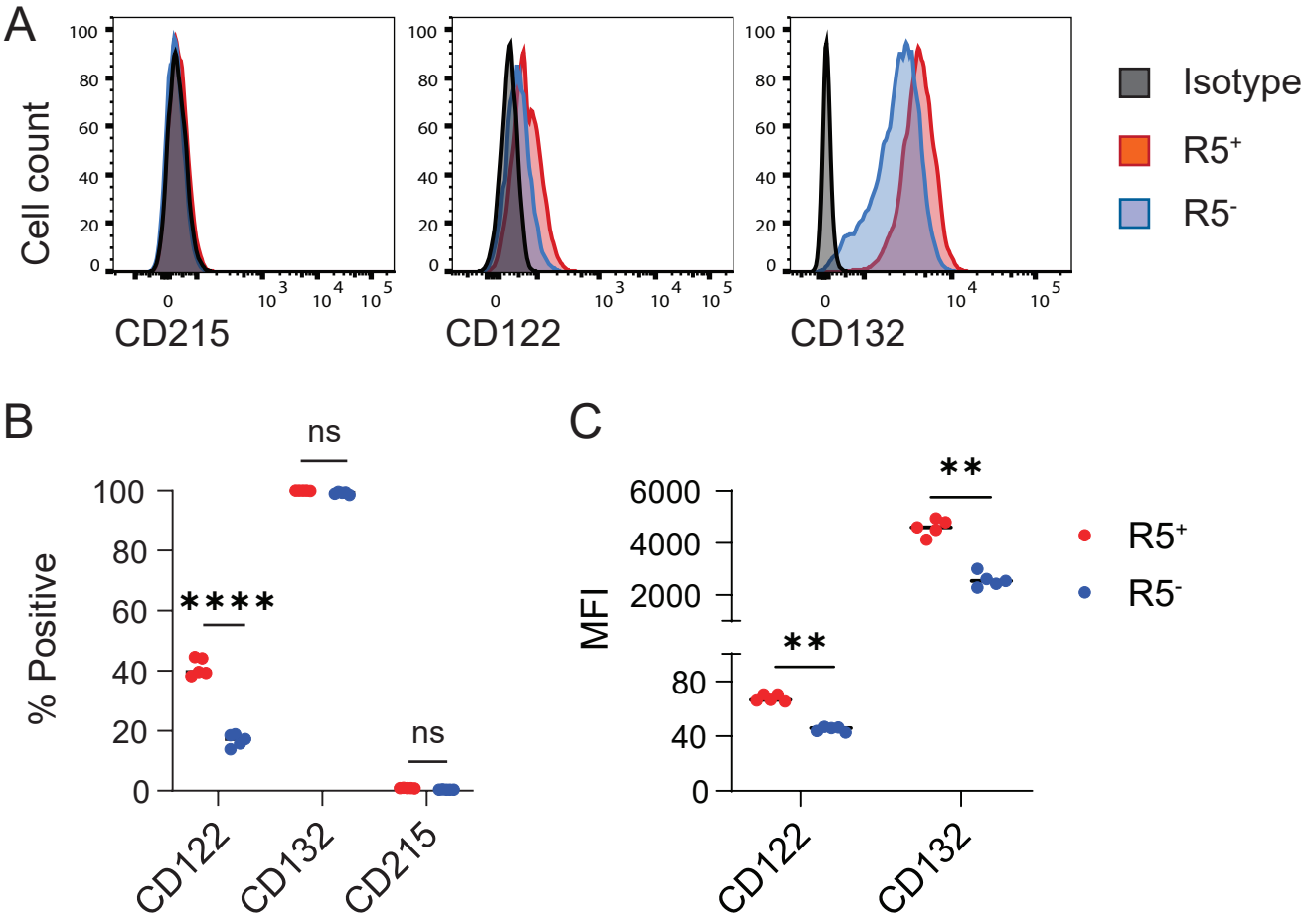


Fig. S1



Supplemental Figure 1. CCR5⁺CD4⁺ T cells are effector or effector memory cells.
Expression of CD45RO and CCR7 in unstimulated CCR5⁺ and CCR5⁻CD4⁺ T cells. CD4⁺ T cells from 7 healthy blood donors were included.

Fig. S2

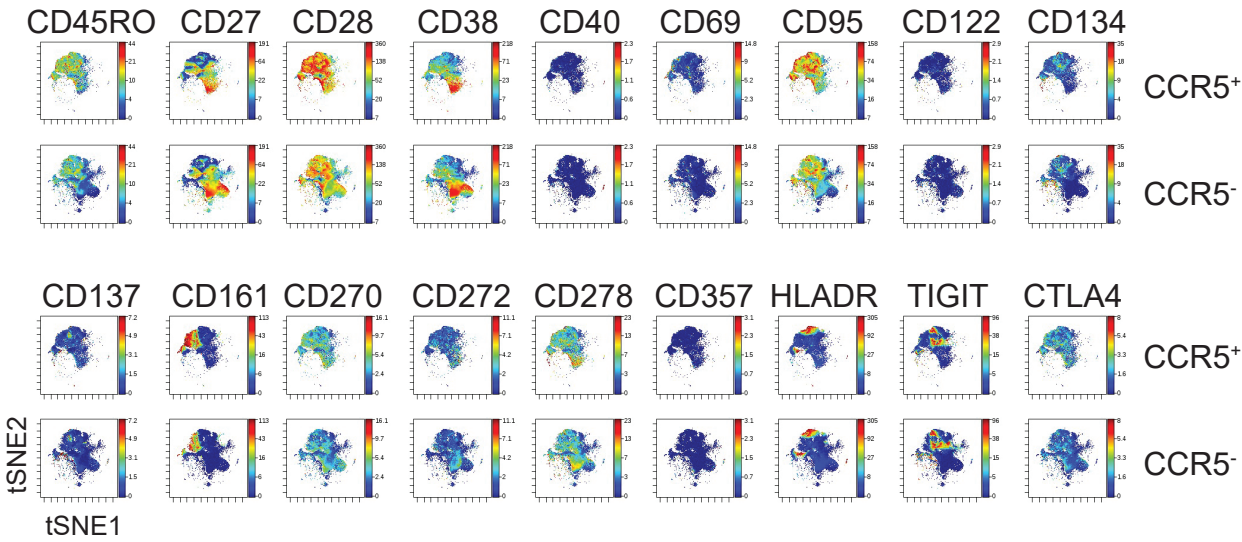


Supplemental Figure 2. Expression of IL15 receptor subunits.

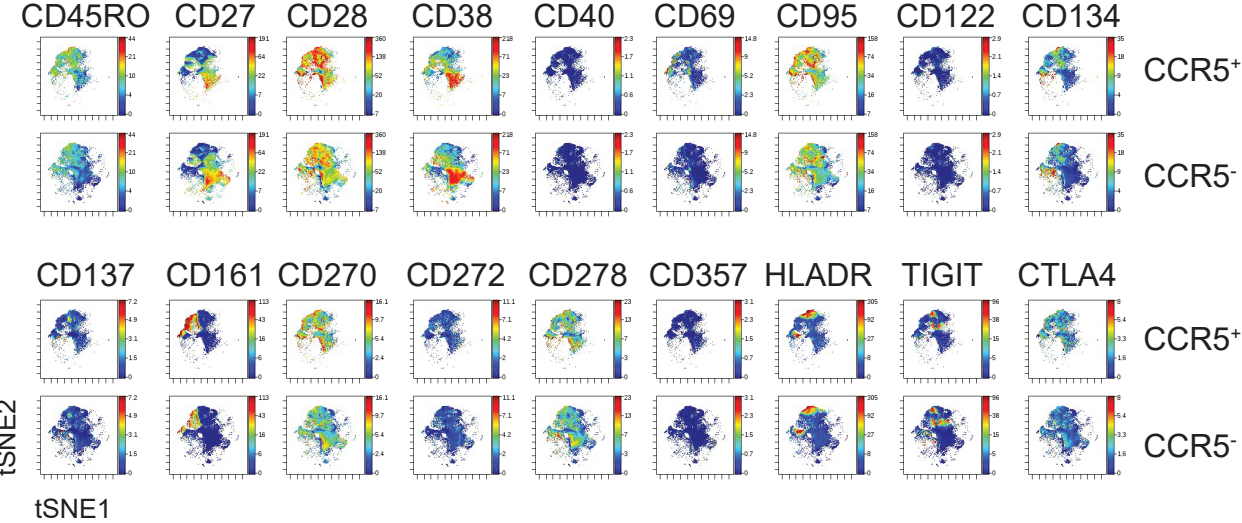
(A-C) Total CD4⁺ T cells isolated from peripheral blood of five healthy donors were stimulated with anti-CD3 and anti-CD28 antibodies for 3 days. Activated cells were cultured for 3 additional days without any cytokine before flow cytometry analysis. *p* values were calculated using two-way ANOVA and Holm-Sidak multiple comparisons test. *** *p* < 0.001; **** *p* < 0.0001.

Fig. S3

Donor 1



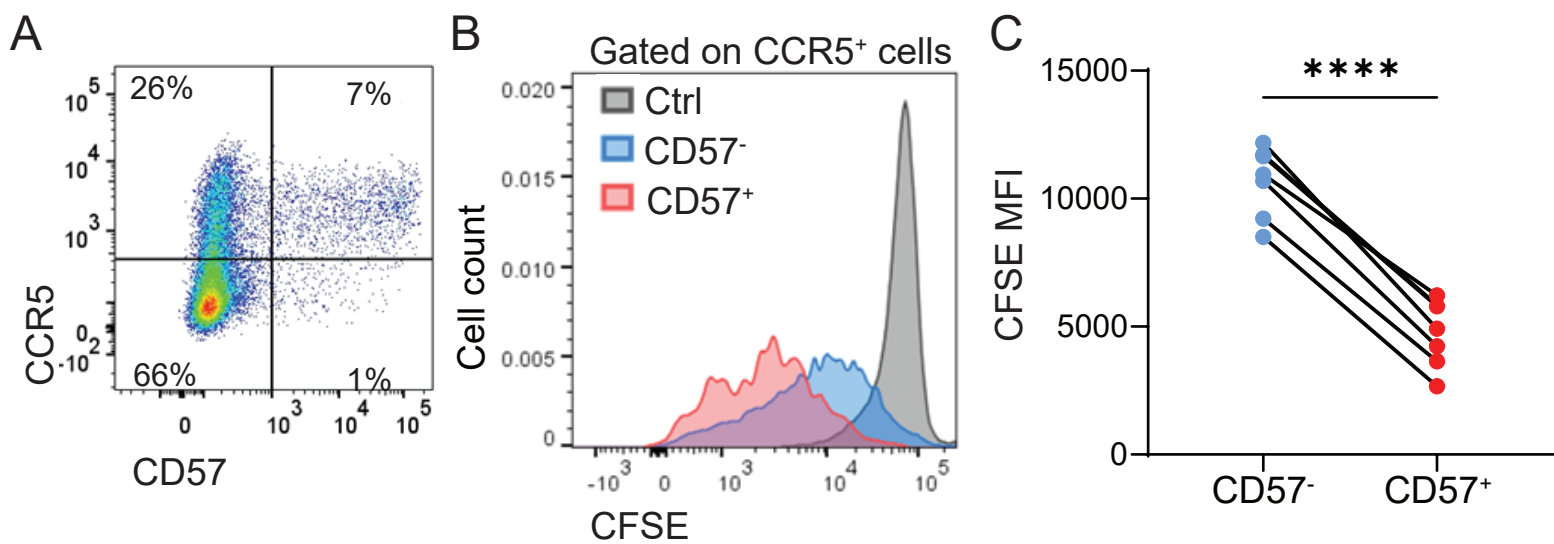
Donor 2



Supplemental Figure 3. CyTOF analysis of CD4⁺ T cells expanded by IL15.

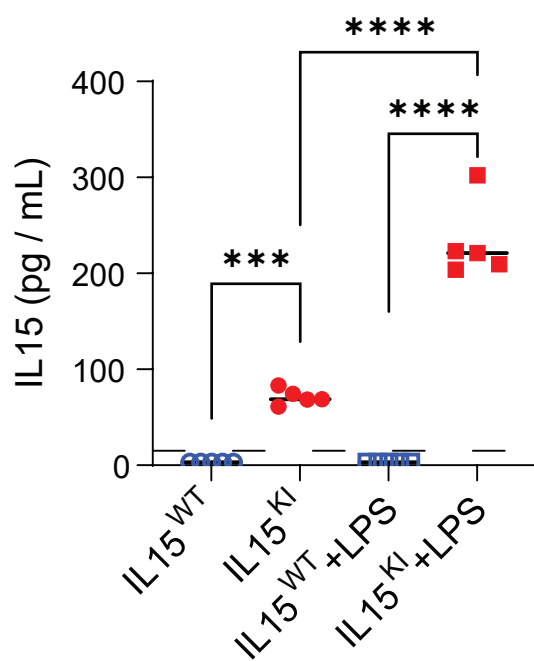
Total CD4⁺ T cells isolated from peripheral blood of two healthy donors were stimulated with anti-CD3 and anti-CD28 antibodies for 3 days. Activated cells were incubated with IL15 for 6 days before CyTOF analysis. Live CD45⁺ singlets were exported for analysis by visualization of stochastic neighbor embedding (viSNE) analysis methods. The viSNE plots illustrate the expression intensity of indicated genes in CCR5⁺ or CCR5⁻CD4⁺ T cells. The coloration is proportional to the expression intensity (blue = low, red = high).

Fig. S4



Supplemental Figure 4. Proliferation of the CD57⁺ subset of CCR5⁺CD4⁺ T cells driven by IL15. Total CD4⁺ T cells isolated from peripheral blood of seven healthy donors were co-stimulated with anti-CD3 and anti-CD28 antibodies for 3 days. Activated cells were stained with CFSE and incubated with IL15 for 6 days before flow cytometry analysis. **(A)** Most CD57-expressing cells are CCR5⁺. **(B-C)** IL15 expands the CD57⁺ subset of CCR5⁺ cells. *p* values were calculated using paired t test. **** *p* < 0.0001.

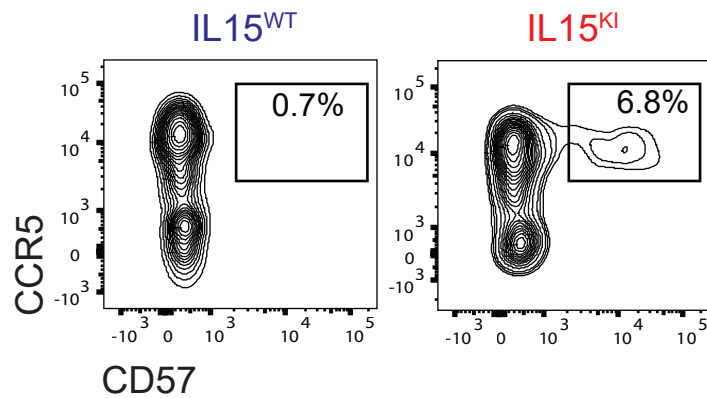
Fig. S5



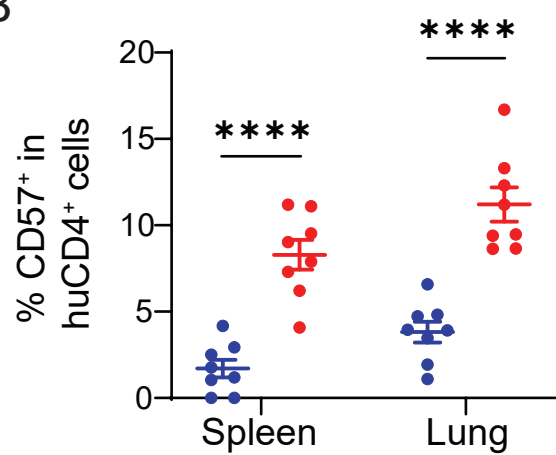
Supplemental Figure 5. Human IL15 concentration in IL15^{KI} mice. Human IL15 measured in the plasma of IL15^{KI} and IL15^{WT} mice following LPS treatment (0.4mg/kg). *p* values were calculated using one-way ANOVA with Tukey test, ****p* < 0.001, *****p* < 0.0001. Detection limit is 3.91pg /mL. Open symbols represent no detection.

Fig. S6

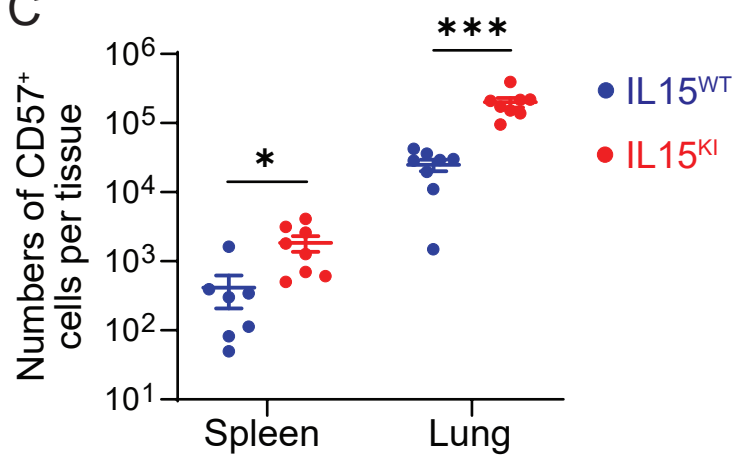
A



B



C



Supplemental Figure 6. Expansion of the CD57⁺ subset of CCR5⁺CD4⁺ T cells in IL15^{KI} mice.

Total CD4⁺ cells from blood were co-stimulated with anti-CD3 and anti-CD28 antibodies for 3 days before transfused into IL15^{WT} and IL15^{KI} mice by retro-orbital injection. Each mouse received 5*10⁶ cells. Blood and tissues were collected on day 6 post transfusion for flow cytometry analysis. **(A)** Expression of CD57 in CD4⁺ T cells in lungs of IL15^{WT} and IL15^{KI} mice. **(B-C)** The percentage (B) and number (C) of human CD57⁺ cells in spleens and lungs from IL15^{WT} and IL15^{KI} mice. *p* values were calculated using two-way ANOVA and Holm-Sidak multiple comparisons test. * *p* < 0.05; *** *p* < 0.001; **** *p* < 0.0001.