Supplemental Figure 1: Mll1 is required for proper differentiation of early T_FH.

(A) TPM values for *Mll1* and in naïve, T_FH and T_H1 CD4 T cells. Data is from the indicated papers.
(B) Expression of TBP and Mll1 in shRNA+ SMARTA CD4 T cells *in vitro*. (C-F) shRNA+ SMARTA CD4 T cells were transferred into C57BL/6 mice and analyzed 3 days after infection with LCMV-Arm. CXCR5+CD25- T_FH and CXCR5-CD25+ T_H1 (C) and CXCR5+Bcl6+ T_FH (D) in SMARTA CD4 T cells. (E, F) Flow plots and quantitation of SMARTA CD4 T cells. (G) Expression of TBP and Mll1 in gRNA+ Cas9^Tg SMARTA CD4 T cells *in vitro*. (H-I) gRNA+ Cas^Tg SMARTA CD4 T cells were transferred into C57BL/6 mice and analyzed 3 days after infection with LCMV-Arm. CXCR5+CD25- T_FH and CXCR5-CD25+ T_H1 (H) and CXCR5+Bcl6+ T_FH (I) in Cas^Tg SMARTA CD4 T cells. (J) Quantitation of Cas^Tg SMARTA CD4 T cells. (K) Flow plots and quantitation of shRNA+ SMARTA CD4 T cells transferred into C57BL/6 mice and analyzed 6 days after infection with LCMV-Arm. Data shown are from one experiment representative of 1 (B, G), 4 (C-F), 3 (G-I) or 5 (K) independent experiments with 3-4 mice per group. *p ≤ 0.05 (unpaired two-tailed Student's t-test).
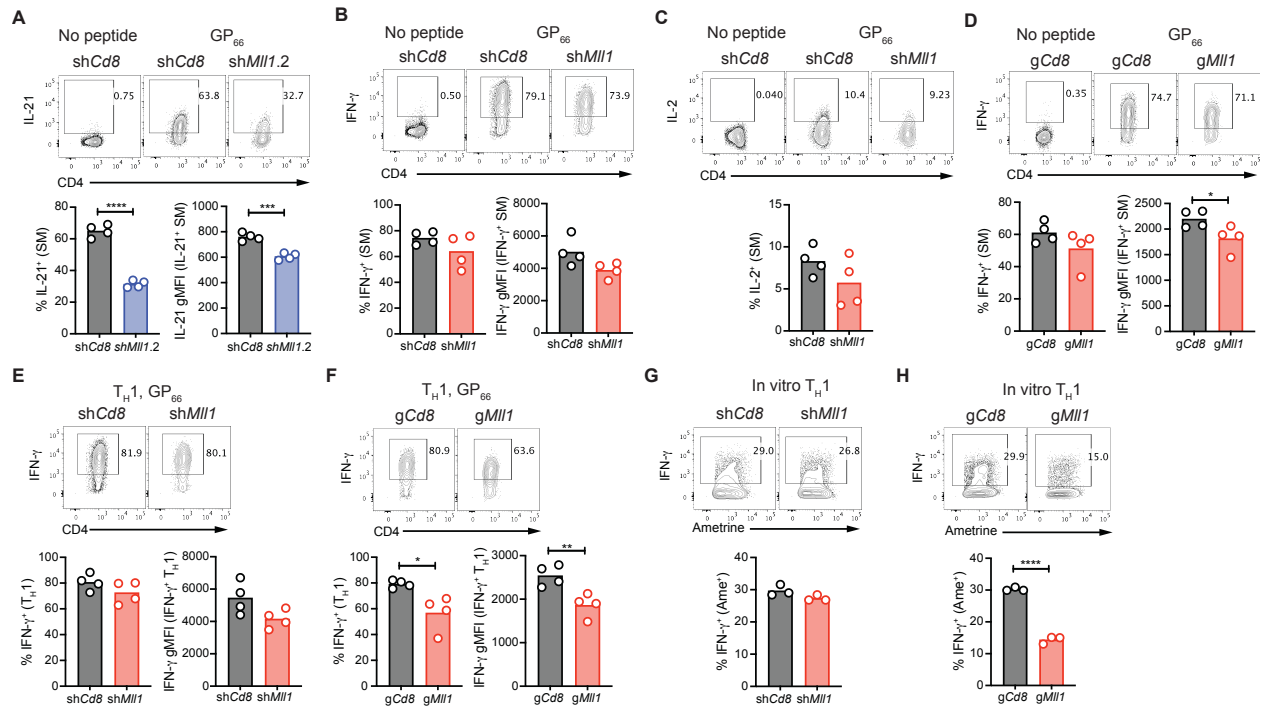
Supplemental Figure 2: Mll1 is required for IL-21 production.

(A-C, E) shRNA$^+$ SMARTA CD4 T cells were transferred into C57BL/6 mice. 6 days after infection with LCMV-Arm, splenocytes were restimulated with LCMV gp$_{66-77}$ peptide. Expression of IL-21 (A), IFN-γ (B) or IL-2 (C) in SMARTA CD4 T cells and of (E) IFN-γ in T$_H$1 SMARTA CD4 T cells. (D, F) gRNA$^+$ Cas9^{Tg} SMARTA CD4 T cells were transferred into C57BL/6 mice. 6 days after infection with LCMV-Arm, splenocytes were restimulated with LCMV gp$_{66-77}$ peptide. Expression of (D) IL-21 in Cas9^{Tg} SMARTA CD4 T cells and of (F) IFN-γ in T$_H$1 Cas9^{Tg} SMARTA CD4 T cells. (G) Expression of IFN-γ in shRNAmir$^+$ CD4 T cells cultured in T$_H$1 conditions and restimulated with anti-CD3. (H) Expression of IFN-γ in gRNA$^+$ Cas9^{Tg} SMARTA CD4 T cells cultured in T$_H$1 conditions and restimulated with anti-CD3. Data shown are from one experiment representative of 5 (A, B, E, F) or 2 (C, D, G-H) independent experiments with 3-4 mice per group. *p $\leq$ 0.05, **p $\leq$ 0.01, ***p $\leq$ 0.001, ****p $\leq$ 0.0001 (unpaired two-tailed Student's t-test).
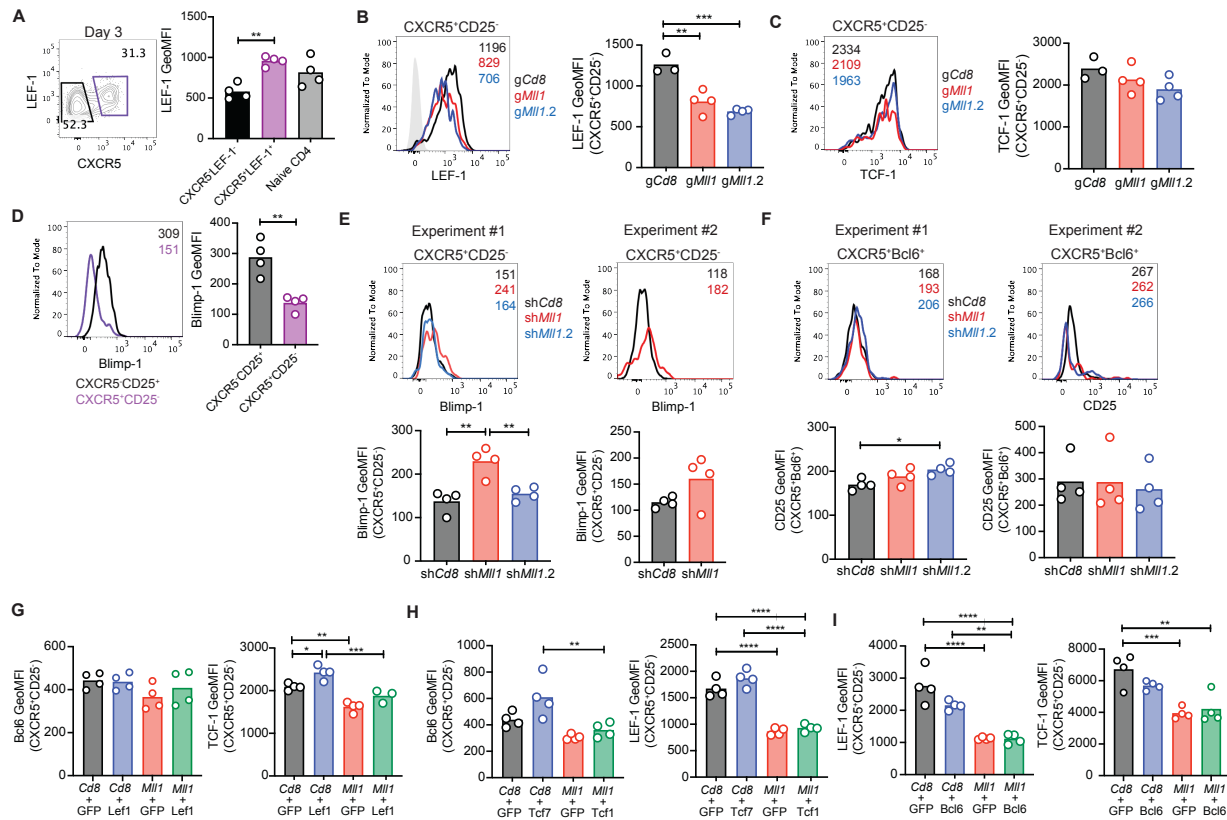
Supplemental Figure 3: Mll1 regulates expression of LEF-1, TCF-1 in T$_{FH}$ cells.

shRNA$^+$ SMARTA (A, D-F), gRNA$^+$ Cas9^{Tg} SMARTA (B, C) or shRNA$^+$RV$^+$ SMARTA (G-I) CD4 T cells were transferred into C57BL/6 mice and analyzed 3 days after infection with LCMV-Arm. (A) Expression of CXCR5 and LEF-1 in sh$Cd8^+$ SMARTA CD4 T cells and quantitation of LEF-1 expression. (B-C) Histogram and quantitation of LEF-1 (B) and TCF-1 (C) expression in Cas9^{Tg} SMARTA CXCR5$^+$CD25$^-$ T$_{FH}$. Numbers in the histograms indicate geometric MFI values. (D) Histogram and quantitation of Blimp-1 expression in CXCR5$^-$CD25$^+$ and CXCR5$^+$CD25$^-$ sh$Cd8^+$ SMARTA CD4 T cells. Numbers in the histogram indicate geometric MFI values. (E) Histogram and quantitation of Blimp-1 expression in CXCR5$^+$CD25$^-$ SMARTA CD4 T cells for two independent experiments. Numbers in the histograms indicate geometric MFI values. (F) Histogram and quantitation of CD25 expression in CXCR5$^+$Bcl6$^+$ SMARTA CD4 T cells for two independent experiments. Numbers in the histograms indicate geometric MFI values. (G-I). Quantitation of Bcl6, TCF-1 or LEF-1 expression in CXCR5$^+$CD25$^-$ SMARTA CD4 T cells. Data shown are from one experiment representative of 2-3 independent experiments with 4 mice per group (A-D, G-I). (D) **p $\leq$ 0.01 (unpaired two-tailed Student's t-test). (A, B, C, E-I) *p $\leq$ 0.05, **p $\leq$ 0.01, ***p $\leq$ 0.001, ****p $\leq$ 0.0001 (one way ANOVA with Tukey's multiple comparisons test.