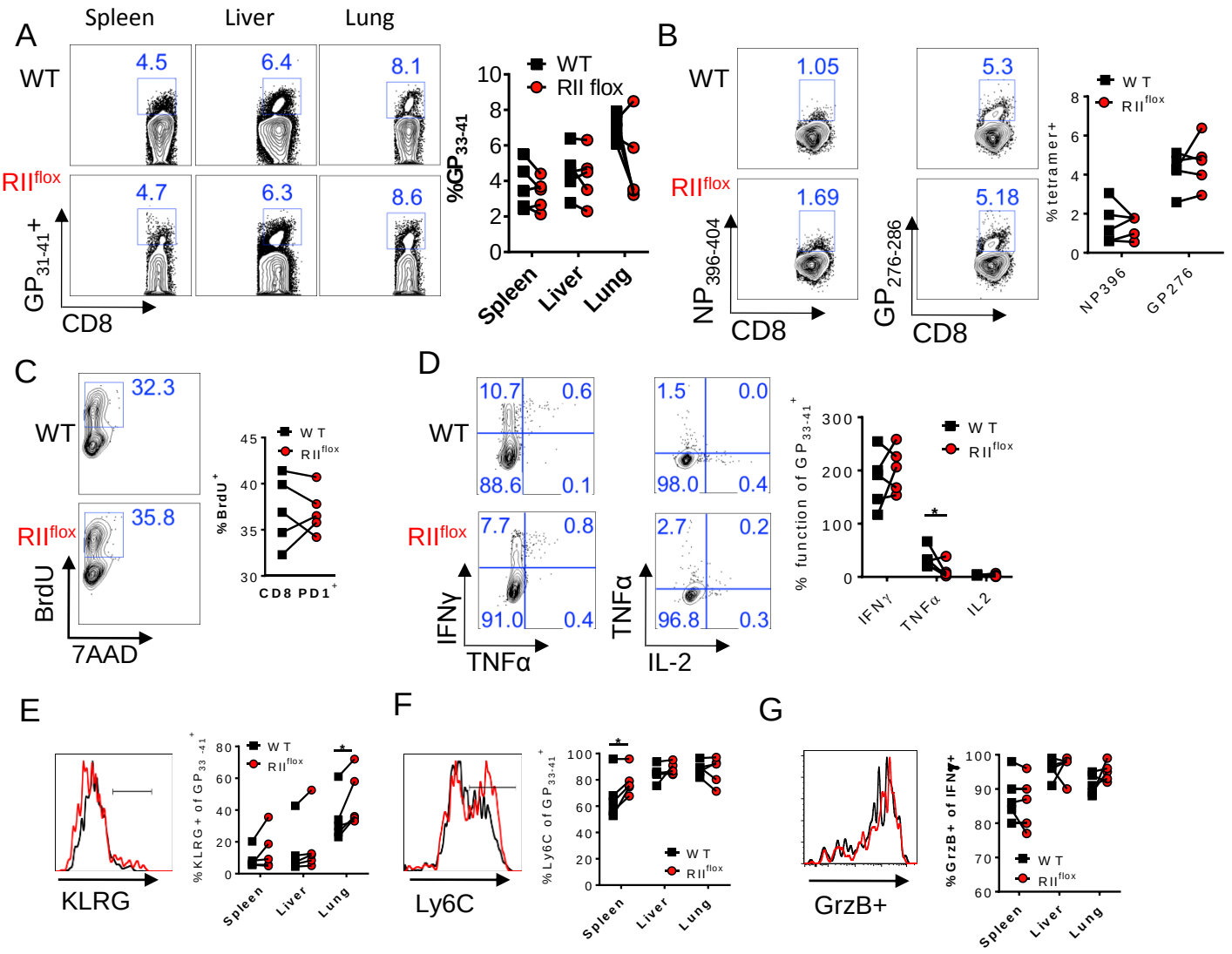

Figure S1. Cell-intrinsic TGFβRII signaling minimally impacts antiviral CD8 T cell responses early after chronic LCMV infection. Reconstituted 1:1 mix of WT(CD45.1, black) and ERcre^{+}TGFβRII$^{flox/flox}$ (RII^{flox}-CD45.2, red) bone marrow chimeric mice were tamoxifen treated, rested, and infected with 2x10^{6} PFU of LCMV Cl13. Spleens and tissues were analyzed 9 days p.i. for the presence of LCMV specific CD8 T cells by flow cytometry. **A)** Percentage of D^{b}:GP_{33-41} CD8 T cells after gating on CD8 T cells from donor compartments in indicated tissue. **B**) Percentage of D^{b}:$NP_{396-404}$ and D^{b}:$GP_{276-286}$ specific LCMV CD8 T cells in the spleen. **C)** Incorporation of BrdU after 16 hour pulse in splenic CD8 PD1^{+} T cells from either WT or ERcre+ TGFβRII$^{flox/}$ compartment. **D)** Production of intracellular IFNγ, TNFα, IL-2 after 5 hr stimulation with GP_{33-41} cognate peptide, graphed as percentage of D^{b}:GP_{33-41} cells from (A). **E-G)** Percentages of virus specific D^{b}:GP_{33-41}^{+} cells expressing KLRG, Ly6C and GranzymeB. Representative of 3 independent experiments of n=4-5 mice/exp. Paired t-test: *p<0.05, **p<0.005.

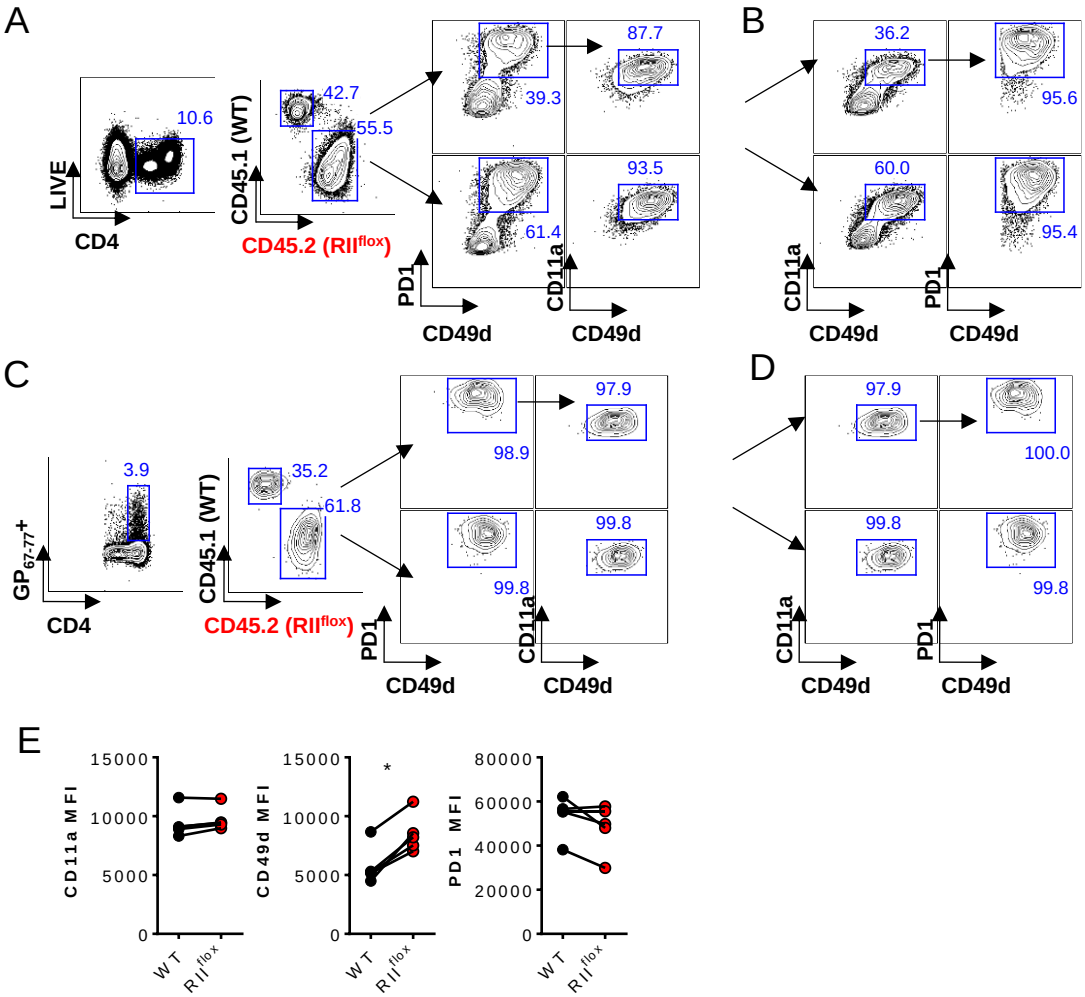

Figure S2. CD11a$^+$ CD49d$^+$ cells and PD1$^+$ cells are overlapping populations in total and virus-specific CD4 T cells during chronic LCMV infection. 8 weeks post-bone marrow reconstitution with 1:1 mix of WT(CD45.1, black) and ERcre$^+$ TGFβRII$^{flox/flox}$ (RII^{flox}-CD45.2, red) bone marrow, mice were tamoxifen treated and infected with 2x10^6 PFU of LCMV Cl13. Spleens were analyzed 9 days p.i. by flow cytometry. **A-B)** Percentage of CD4 T cells from each compartment that co-express PD1, CD11a and CD49d first gating on PD1$^+$ cells (a) or first gating on CD11a$^+$ CD49d$^+$ cells (b). **C-D)** Percentage of I-A^b-GP$_{67-77}$ tetramer$^+$ CD4 T cells from each compartment that co-express PD1, CD11a and CD49d first gated on PD1$^+$ cells (c) or first gating on CD11a and CD49d (d). **E)** MFI of indicated marker on I-A^b-GP$_{67-77}$ tetramer$^+$ CD4 T cells from (c). Representative of 2 independent experiments of n=4-5 mice/group. Paired t-test *p<0.05, **p<0.005, ***p<0.0005.

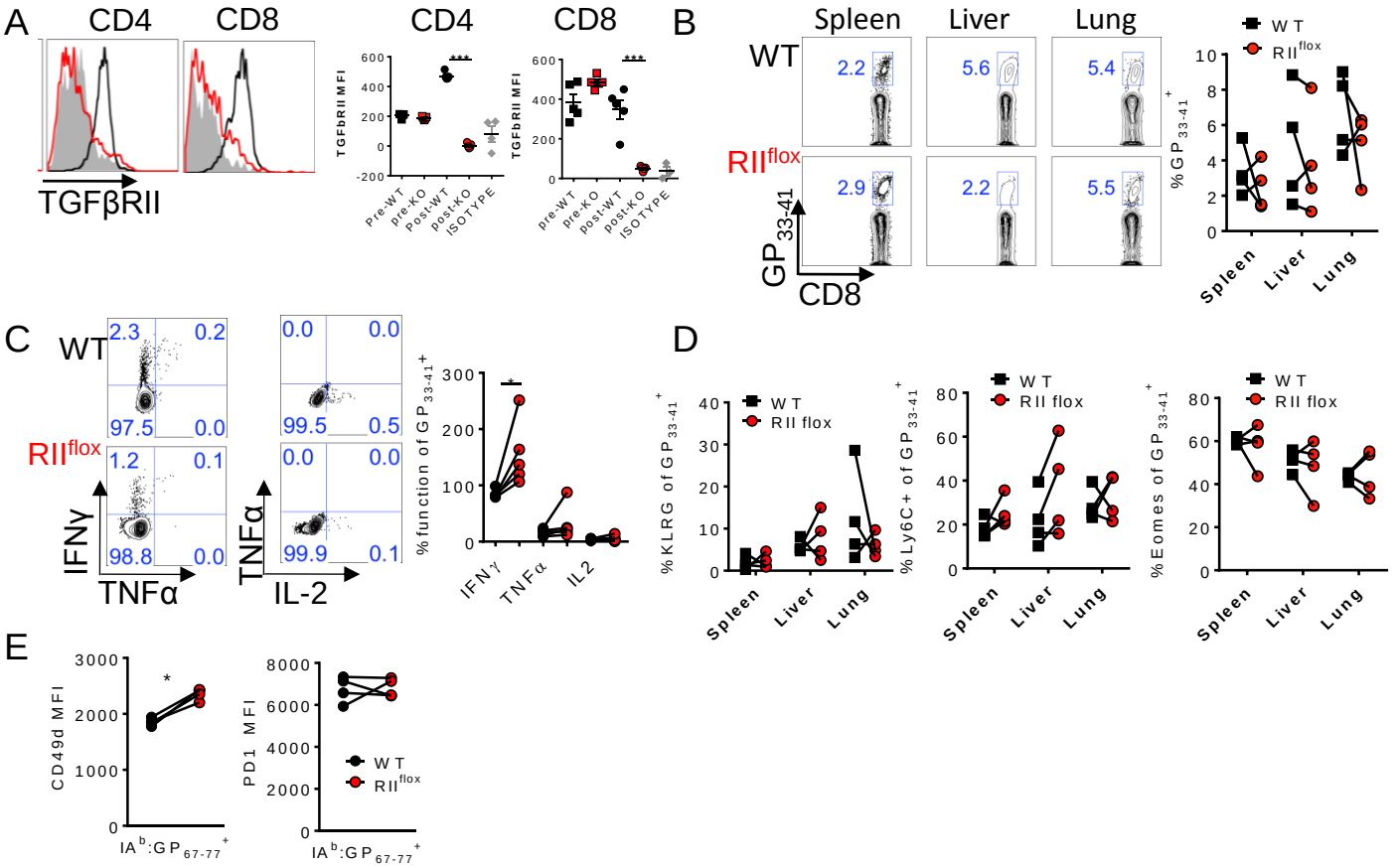

Figure S3. Cell-intrinsic TGFβRII signaling in adults does not limit LCMV-specific CD8 T cell responses late after chronic infection. A-D) Reconstituted 1:1 mix of WT(CD45.1, black) and ERcre^{+}TGFβRII$^{flox/flox}$ (RII^{flox}-CD45.2, red) bone marrow chimeras mice first infected with 2x10^{6} PFU of LCMV Cl13 then tamoxifen treated days 12-17p.i. and spleens analyzed at day 30 p.i. for the presence of LCMV specific T cells. **A)** TGFβRII expression in T cells post-tamoxifen over isotype (gray). **B**) Percentage D^{b}:GP$_{31-41}$$^{+}$ of CD8 T cells in indicated tissues. **C)** Co-production of intracellular IFNγ and TNFα or TNFα and IL-2 after 5 hr stimulation with GP$_{33-41}$ peptide, graphed as percent of D^{b}:GP$_{33-41}$$^{+}$ cell from (B). **D)** Expression of KLRG Ly6C and EOMES gated on D^{b}:GP$_{33-41}$$^{+}$ cells from (B). **E)** CD49d and PD1 MFI on CD4^{+} IA^{b}:GP$_{67-77}$$^{+}$ cells from the spleen. Representative of 3 independent experiments of n=4-5 mice/group. Paired t-test , *p<0.05, **p<0.005, ***p<0.0005.

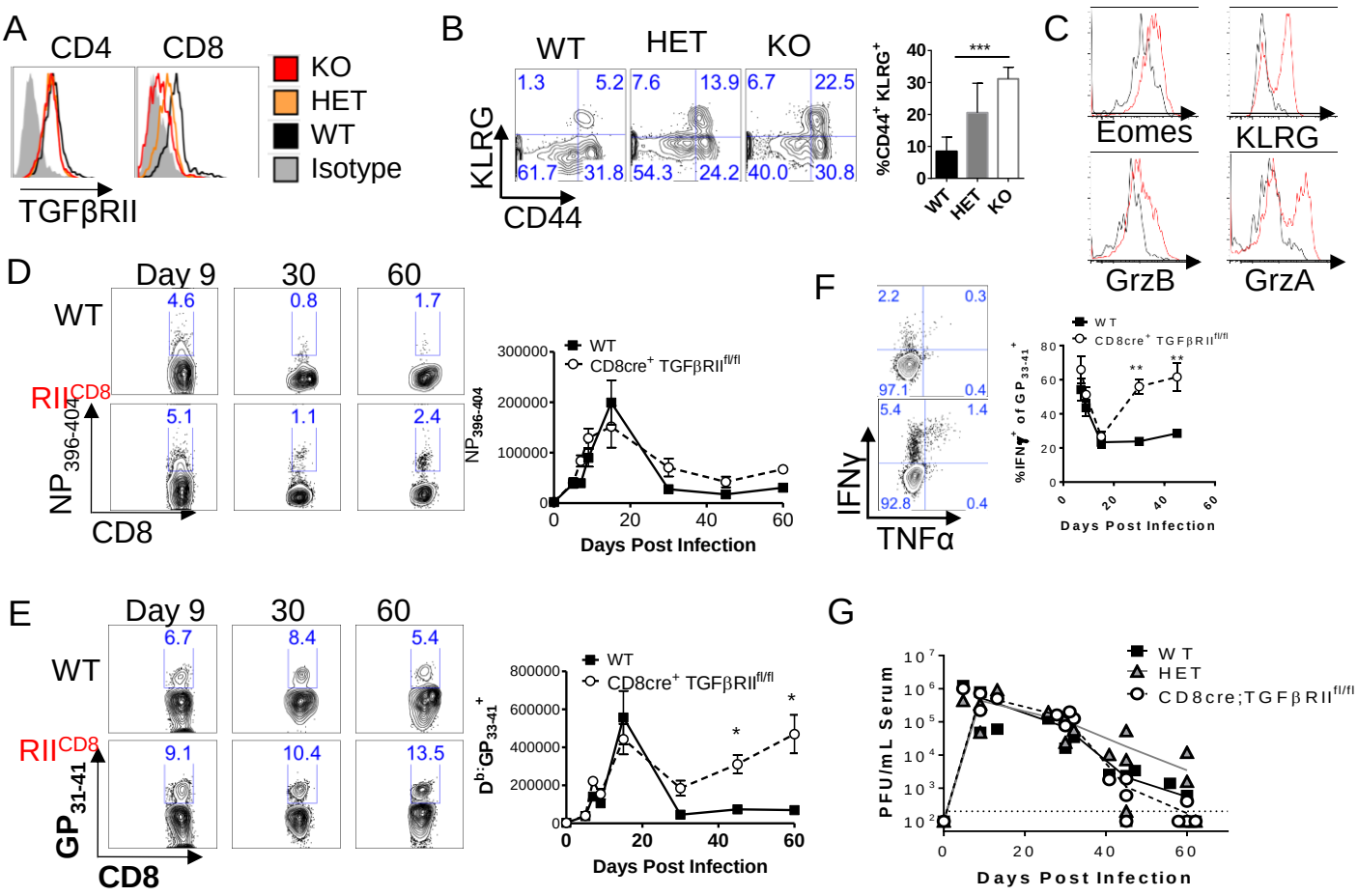

Figure S4. TGFβRII signaling in CD8 T cells from birth does not limit LCMV-specific CD8 T cell responses after chronic infection. CD8cre^{+} TGFβRII$^{flox/flox}$ (RII^{CD8}) mice and Cre- littermate controls infected with 2x10^{6} PFU of LCMV Cl13 and blood monitored. **A**) TGFβRII expression on CD4 T cell and CD8 T cells prior to infection. **B**) Percentage of CD44+ CD8 T cells expressing KLRG prior to infection. **C)** Expression of Eomes, KLRG GrzB and GrzA prior to infection gated on CD44 hi cells. **D)** Number of virus specific D^{b}:NP$_{396-404}$$^{+}$ cells over time post infection. **E)** Number of virus specific D^{b}:GP$_{33-41}$$^{+}$ cells. **F)** IFNγ and TNFα production upon cognate peptide ex-vivo graphed as a percentage of tetramer+ cells from (i). **G)** Viremia over time by plaque assay as PFU/mL serum. Representative of 3 independent experiments of n=4-5 mice/group. Two-way ANOVA, *p<0.05, **p<0.005, ***p<0.0005.

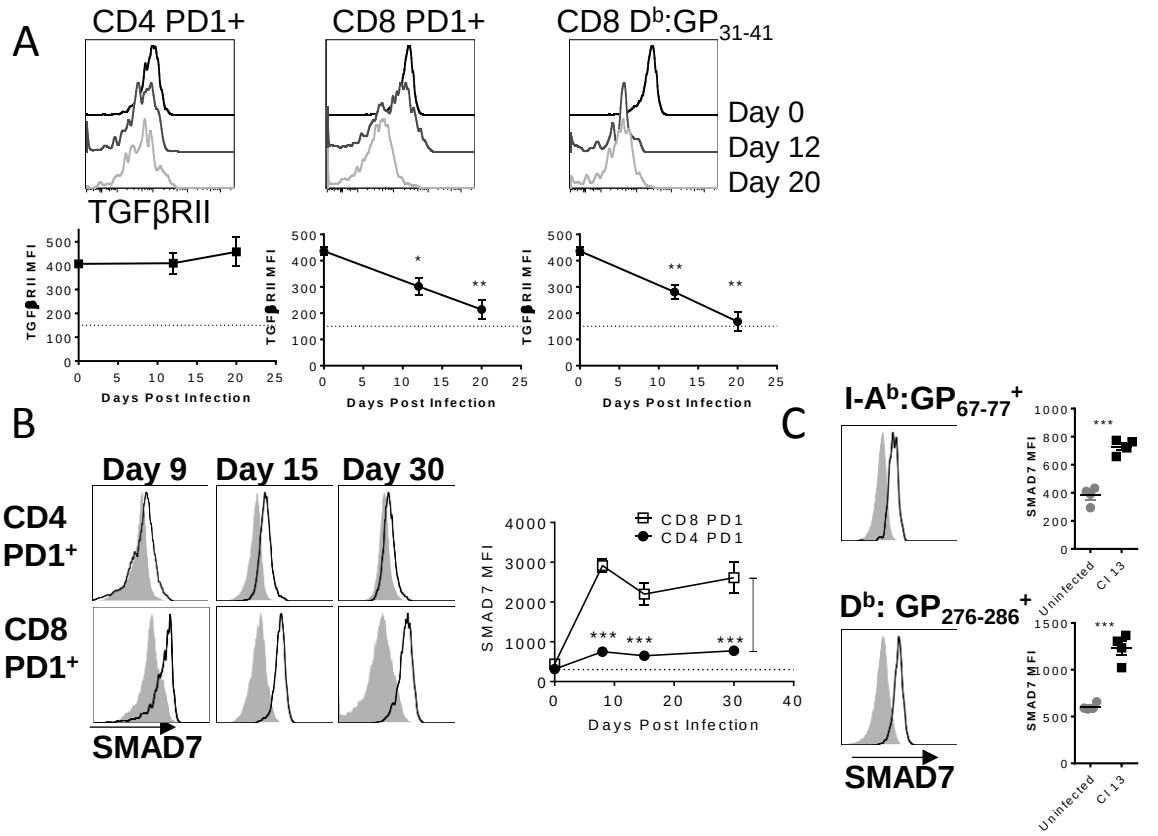

Figure S5. Differential TGFβR and SMAD7 expression in CD4 and CD8 T cells during chronic LCMV infection. C57BL/6 mice were infected with $2x10^6$ PFU LCMV Cl13 i.v. or left uninfected. **A)** Surface TGFβRII expression gated on $CD4^+$ $PD1^+$, $CD8^+$ $PD1^+$, or $CD8^+$ D^b:GP_{33-41}tetramer$^+$ T cells in the blood was determined in uninfected mice (day 0) or at indicated times after LCMV Cl13 infection. **B)** Splenic CD4 $PD1^+$ or CD8 $PD1^+$ T cells from LCMV-Cl13 infected mice (black histograms) were stained for intracellular SMAD7 at indicated days post infection and compared to uninfected mice (grey histograms). SMAD7 MFI in the indicated T cell populations is depicted throughout LCMV Cl13 infection (right graph). **C)** LCMV specific $CD4^+$ I-A^b-GP_{67-77} tetramer$^+$ or $CD8^+$ D^b-$GP_{276-286}$ tetramer$^+$ T cells were stained for SMAD7 at day 8 p.i.. Representative of 2 independent experiments with 3-5 mice/group. Two-way ANOVA, *p<0.05, **p<0.005, ***p<0.0005.

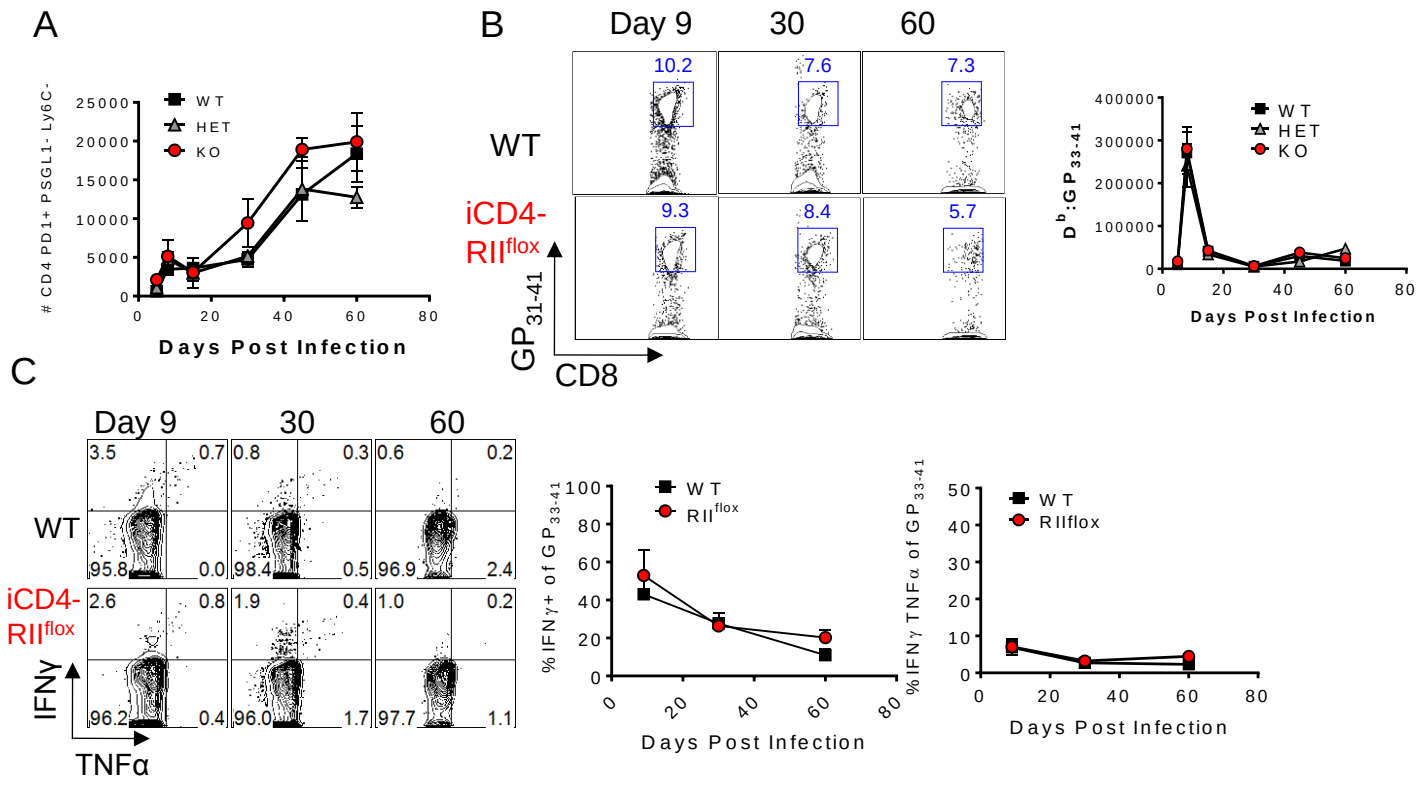

Figure S6. CD4 restricted TGFβRII signaling does not influence circulating PSLG1^{-}Ly6C^{-} CD4 T cells or CD8 T cell responses after chronic viral infection. CD4-ERcre^{+} TGFβRII$^{flox/flox}$ (RII^{flox}) mice and Cre- littermate controls were infected with 2x10^{6} PFU of LCMV Cl13. Blood was monitored for the presence of LCMV specific T cells by flow cytometry. **A)** Number of CD4^{+} PD1 T cells that are PSLG1^{-}Ly6C^{-} Tfh like cells. **B)** Number of virus specific D^{b}:GP$_{33-41}$$^{+}$ cells over time post infection. **C)** IFNγ and TNFα production upon cognate peptide stimulation ex-vivo graphed as a percentage of tetramer+ cells from (b). Representative of 3 independent experiments of n=4-5 mice/group. Two-way ANOVA, *p<0.05, **p<0.005, ***p<0.0005.

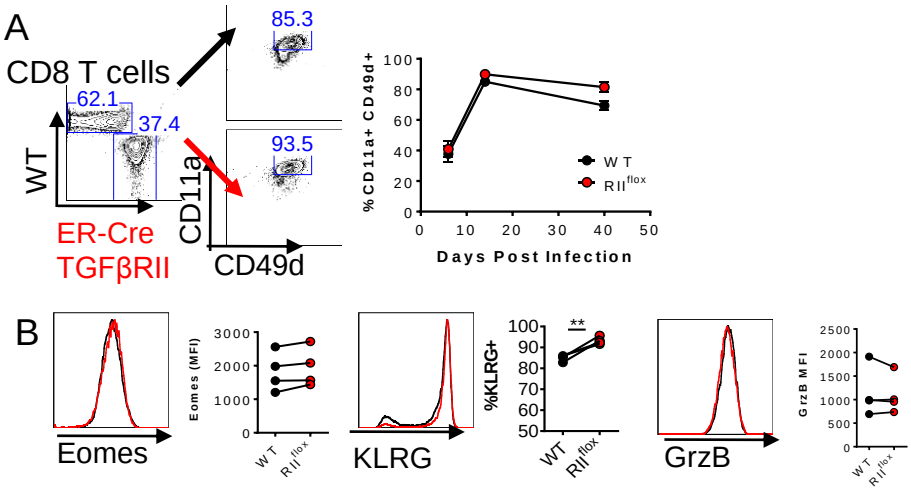

Figure S7. TGFβ suppression of Eomes-driven CD4 T cell responses is common to chronic MCMV infection in-vivo. Mixed chimeras with 1:1 ratio of WT (CD45.1, black) and ERcre^{+} TGFβRII^{flox} (CD45.2, red) BM reconstituted prior to TGFβRII deletion, were infected with 2x10^{4} pfu MCMV i.p.. **A)** Proportion of CD8 T cells expressing activation markers CD11a and CD49d over time after gating on congenic marker, 14 d.p.i.is shown. **B)** Overlays of Eomes, KLRG, and GranzymeB expression in activated CD8 T cells. Representative of 2 independent experiments of n=4-5 mice/group. Two-way ANOVA (a) or paired t-test (b), *p<0.05, **p<0.005.

Supplemental Table 1. Clinical summary of patient samples used.

Donor ID	Sex	Age	Status	HAART	CD4	HIV RNA
1002	M	44	Chronic	No	650	12.143
1007	M	50	Chronic	No	355	11.800
1010	M	39	Chronic	No	383	26.541
1011	M	48	Chronic	No	434	40.300
1012	M	41	Chronic	No	598	75.500
1014	M	29	Chronic	No	402	20.317
1016	M	48	Chronic	No	668	18.144
1017	M	29	Chronic	No	383	99.206
1019	M	48	Chronic	No	753	33.316
1020	M	43	Chronic	No	728	9.536