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Supplemental Information

PD-1 Signaling Promotes Control of Chronic Viral Infection by Restricting Type-I-Interferon-Mediated Tissue Damage

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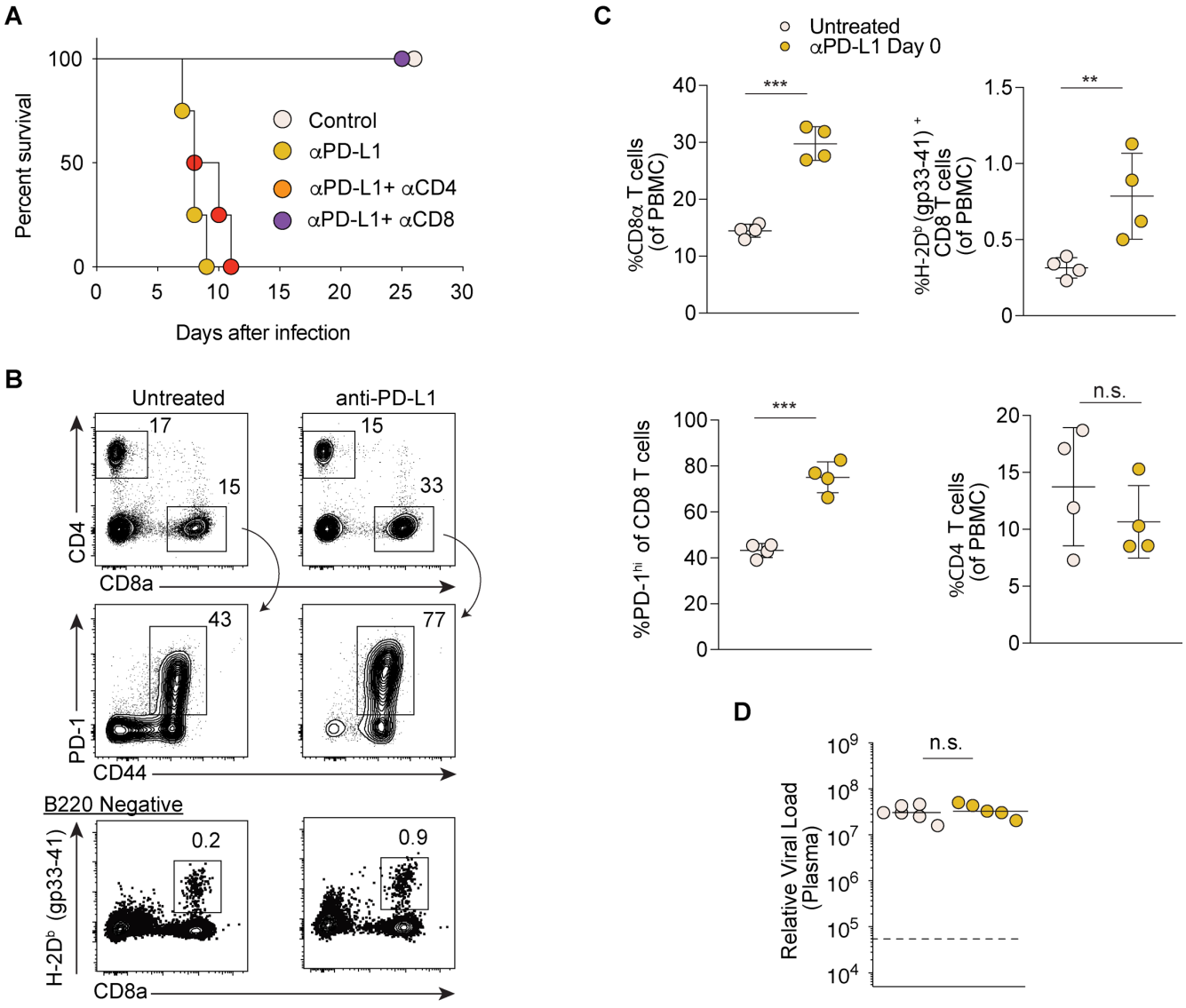

Figure S1. Anti-PD-L1 treatment initiated on day 0 of LCMV-c13 infection results in expansion of CD8 T cells with no impact on viral titer. Related to Figure 1. **(A)** Survival of LCMV-c13 infected mice that were treated with anti-PD-L1 on day 0 in the absence of $CD4^+$ or $CD8^+$ cells. **(B and C)** Expression of CD4, CD8a, CD44, PD-1, and gp33-specific TCR in peripheral blood mononuclear cells of B6 mice on 5dpi of LCMV-c13 with the indicated treatments. Representative plots (B) and data pooled from 3 experiments with n>4 mice per group shown with mean±SD (C). **(D)** Plasma LCMV *gp* transcripts in LCMV-c13-infected B6 mice with indicated antibody treatment on 5 dpi. Data were pooled from 2 independent experiments and shown with median. Statistical analysis tested with the Mann-Whitney U-test.

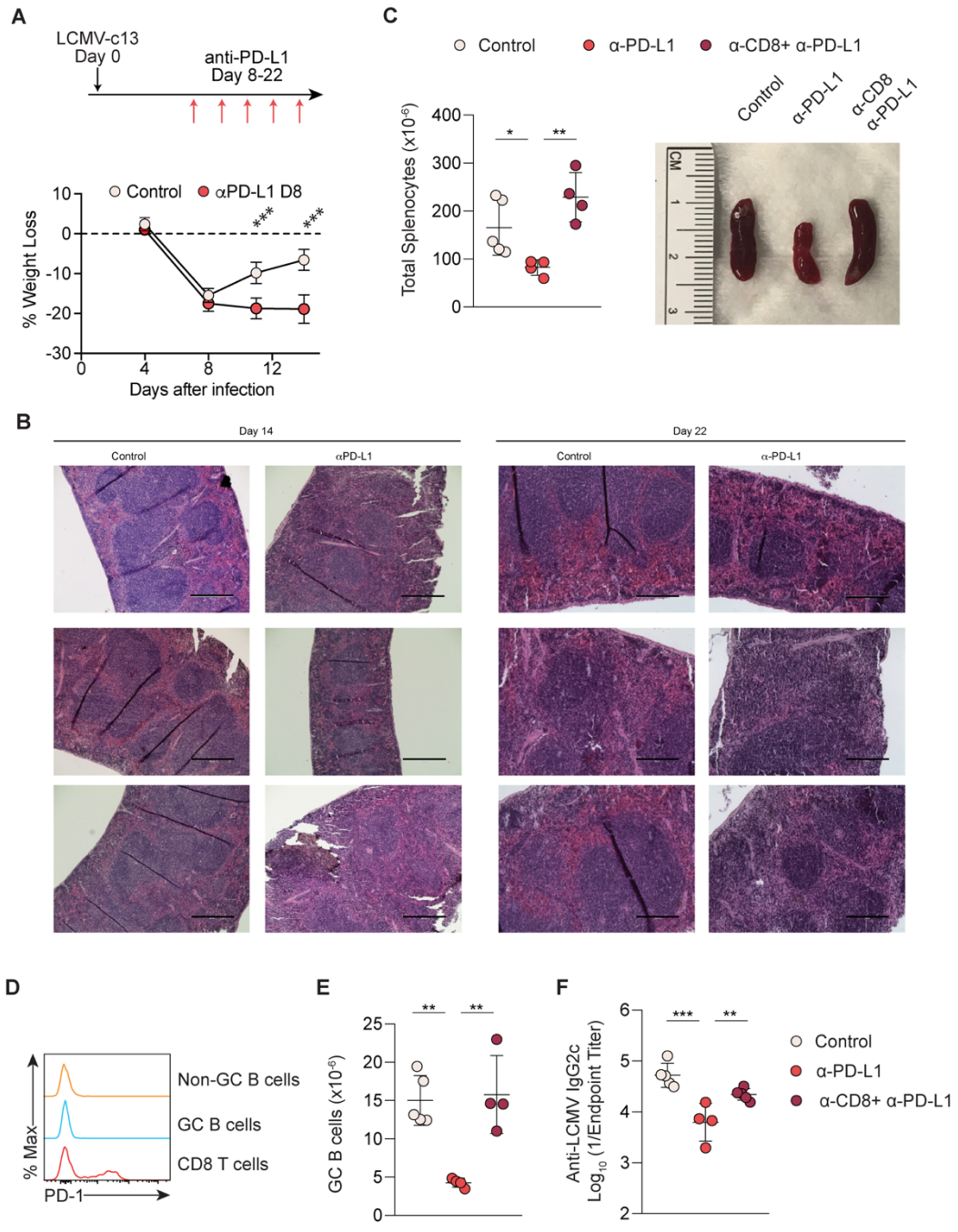

Figure S2. Non-lethal immunopathology following anti-PD-L1 treatment initiated on 8 dpi. Related to Figure 2. **(A)** Change in body weight following LCMV-c13 infection in control and B6 mice with anti-PD-L1 treatment initiated on 8 dpi. **(B)** Hematoxylin and eosin staining of spleen sections from control and day 8-22 anti-PD-L1-treated B6 mice on 14 dpi and 22 dpi as indicated. Scale bars indicate 400 μm. Images are representative of greater than 6 mice per group. **(C)** Splenocyte counts and gross appearance of the spleen of LCMV-c13 infected B6 mice on 22 dpi with treatment with anti-PD-L1 or anti-PD-L1+anti-CD8. **(D)** Expression of PD-1 by Fas^+ $GL7^+$ GC B cells, non-GC B cells and CD8 T cells in LCMV-c13 infected B6 mice on 22 dpi. **(E and F)** Absolute numbers of Fas^+ $GL7^+$ GC B cells in the spleen and anti-LCMV IgG2c antibody titers in the serum of LCMV-c13 infected, anti-PD-L1-treated B6 mice on 22 dpi. Data are pooled from two experiments with n>4 mice per group and shown with mean±SD.

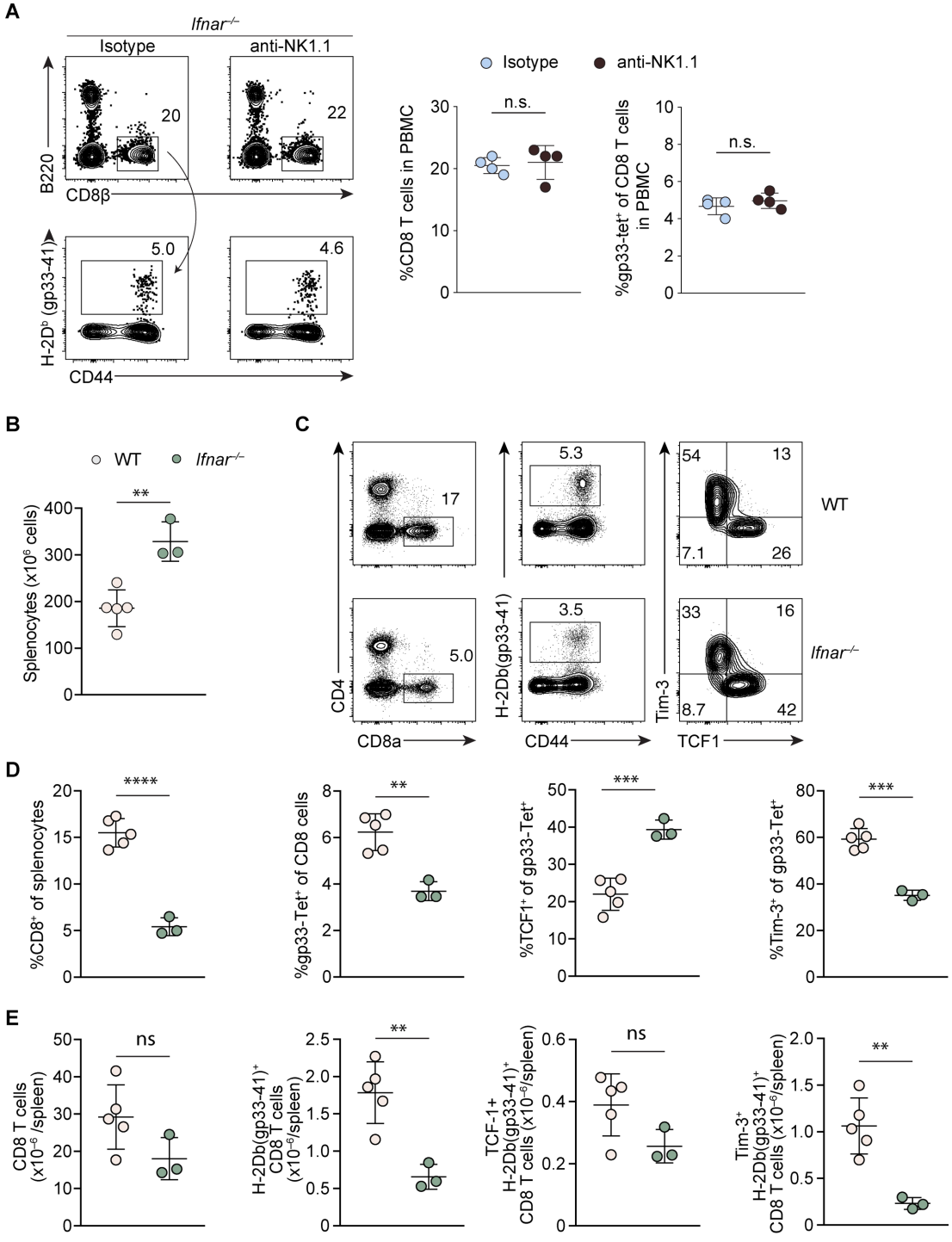

Figure S3. *Ifnar1*$^{-/-}$ mice display increased spleen size, but diminished CD8 T cell responses on 8 dpi of LCMV-c13. Related to Figure 4. **(A)** Frequencies of total and LCMV gp33-specific CD8 T cells in peripheral blood mononuclear cells on 22 dpi in *Ifnar1*$^{-/-}$ mice treated with anti-NK1.1 antibody. Data pooled from 2 experiments and shown with mean±SD. **(B and C)** Splenocyte counts (B) and expression of indicated molecules or tetramer binding by splenocytes (C) of *Ifnar1*$^{+/+}$ (WT, top) and *Ifnar1*$^{-/-}$ (bottom) mice on 8 dpi. Representative plots with the frequencies of cells in each gated population are shown. **(D and E)** Frequencies (D) and absolute numbers (E) of indicated populations in the spleen on 8 dpi pooled from 2 experiments and shown with mean±SD.

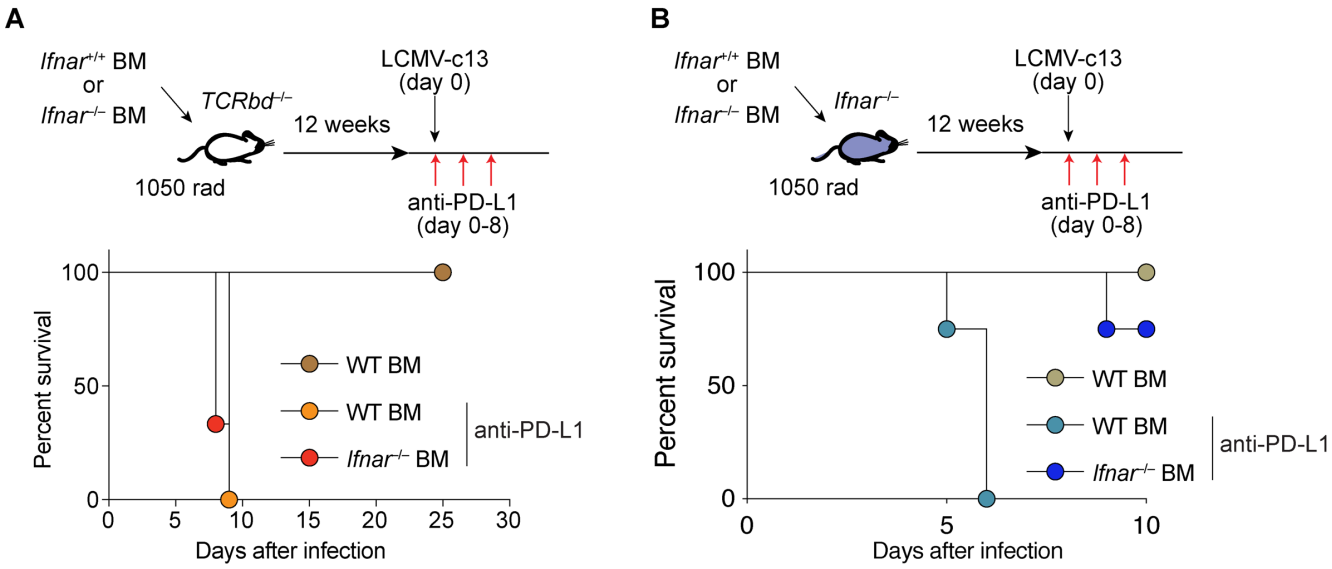

Figure S4. IFNAR signaling in either the hematopoietic or non-hematopoietic compartment is sufficient to cause lethal immunopathology. Related to Figure 4. Survival of *Ifnar1*$^{+/+}$ (A) and *Ifnar1*$^{-/-}$ (B) bone marrow (BM) chimeras reconstituted with *Ifnar1*$^{+/+}$ (WT) or *Ifnar1*$^{-/-}$ hematopoietic cells after infection with LCMV-c13 and treatment with anti-PD-L1 at the beginning of infection as indicated. Data are representative of two experiments with 5 mice in each group.