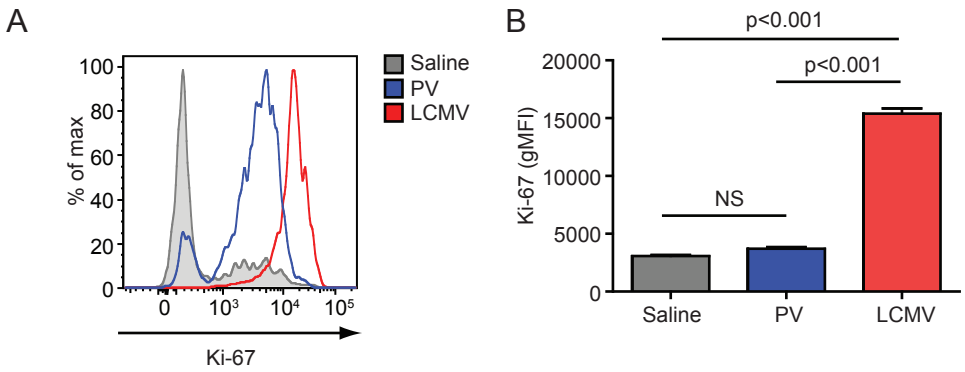
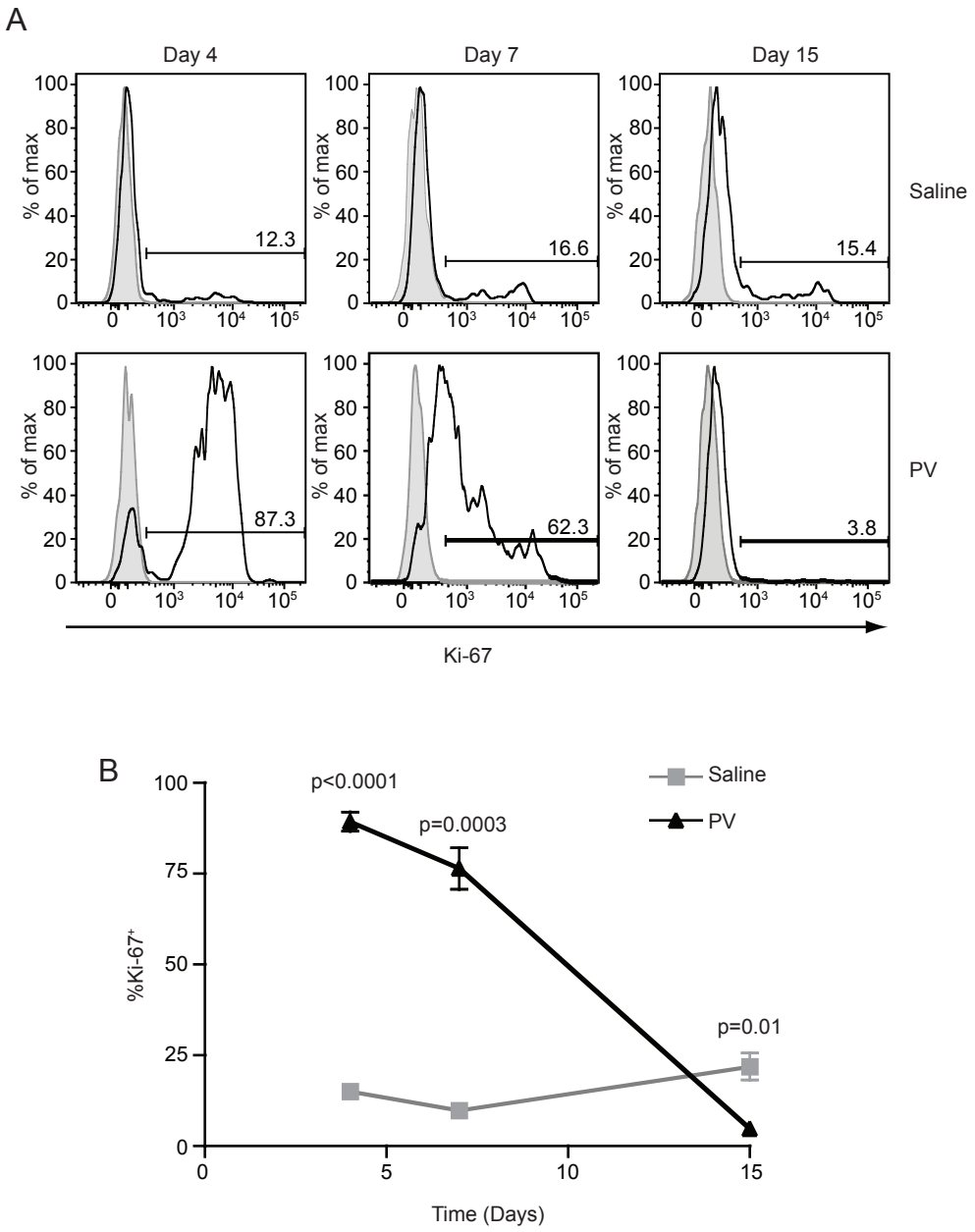
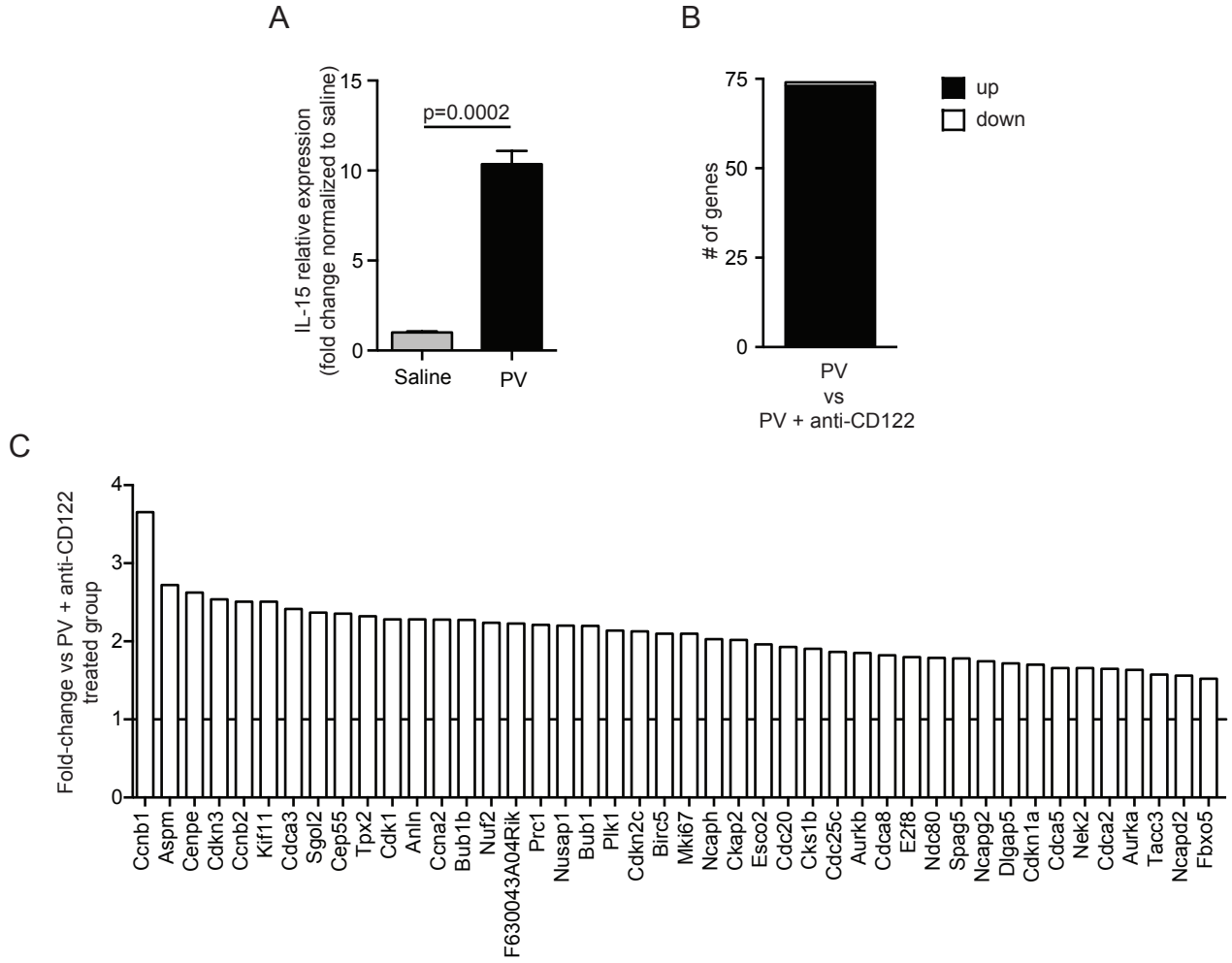


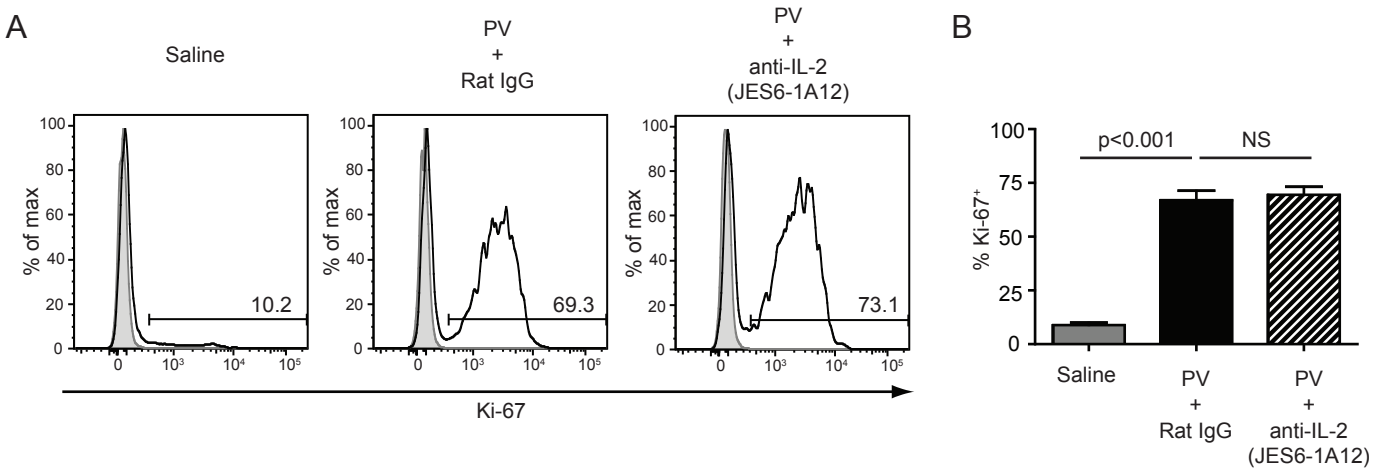
Supplemental Figure 1 : Viral infection induces cell cycle entry of memory CD8⁺ T cells independently of antigen re-encounter. (A) Representative plots of Ki-67 expression by memory P14 cells on day 4 following mock-infection (gray line) or infection with PV (blue line) or LCMV (red line). (B) Cumulative data (mean ± SEM) geometric mean fluorescence intensity (gMFI) of Ki-67 expression by memory P14 cells on day 4 following indicated treatment. Data are from 3 mice per group and representative of 2 independent experiments. Data in (B) were analyzed by One-way ANOVA with Tukey's post-test of multiple comparisons.



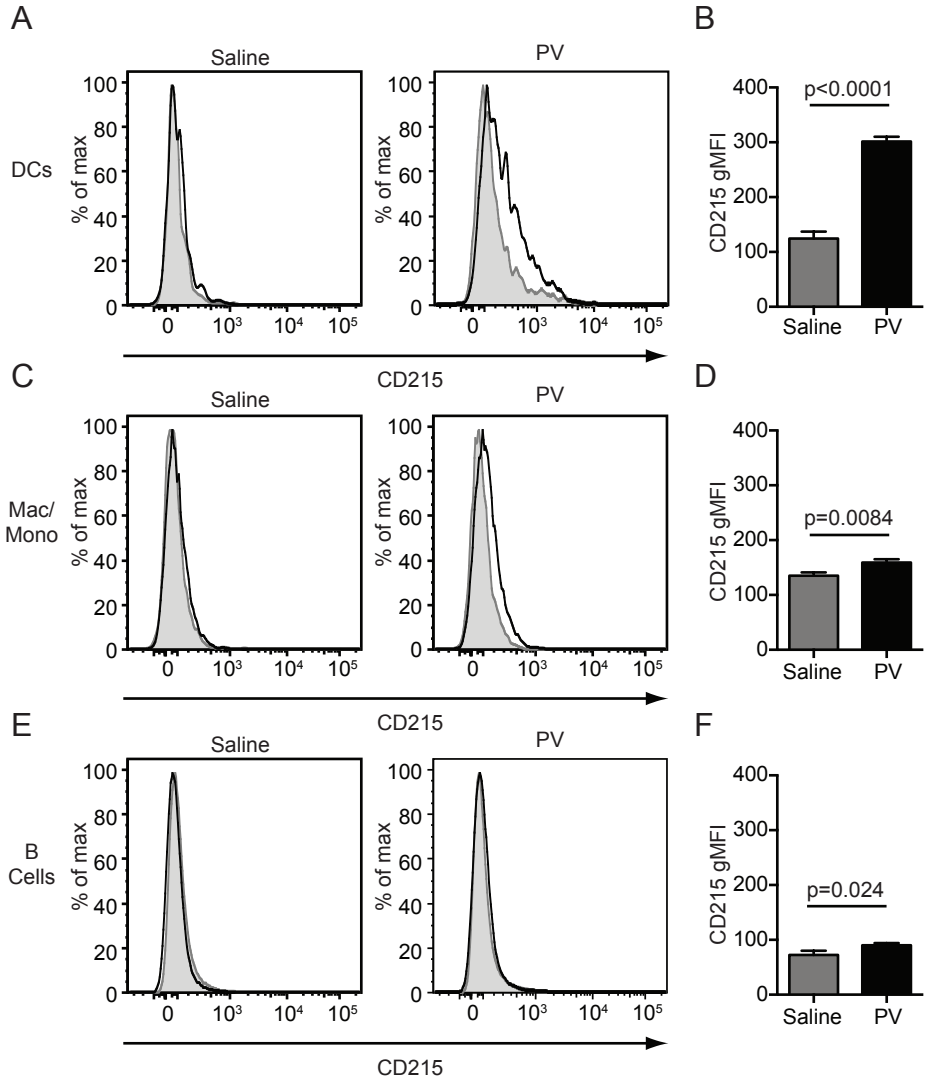
Supplemental Figure 2: Cell cycle entry of memory CD8⁺ T cells following bystander viral infection is transient. (A) Representative plots of Ki-67 expression by memory P14 cells in the blood on the indicated days following PV infection or mock-infection. Shaded histograms are isotype controls. (B) Cumulative data (mean ± SEM) of Ki-67 expression by memory P14 cells on the indicated days following PV infection or mock-infection. Data are from 3 mice that were serially bled on the indicated days and representative of 2 independent experiments. Data in (B) were analyzed by two-tailed, unpaired Student's t-test and significance reflects difference compared to the saline treated group on the same day.



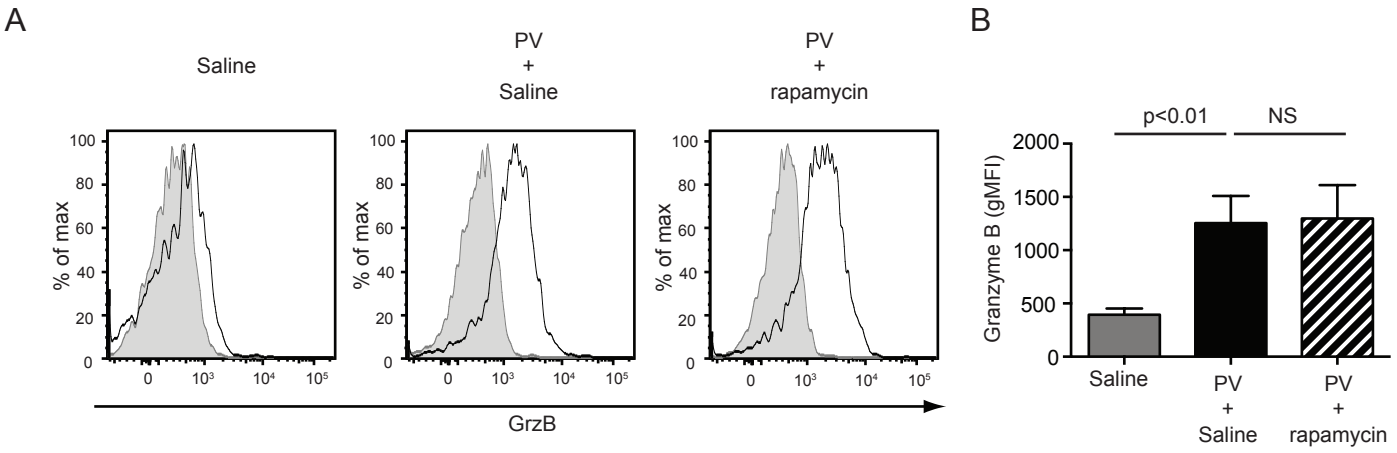
Supplemental Figure 3: Pichinde virus infection induces IL-15 and regulates cell cycle gene expression in an IL-15 dependent manner. (A) Quantification of IL-15 mRNA expression in the spleen on day 2 following pichinde virus infection. Changes in expression were measured using Tata binding protein as a reference genes and normalized to expression in saline treated group. (B) Number of genes differentially expressed ($p<0.01$, fold-change >1.5) in memory P14 cells on day 4 following PV infection compared to PV infection combined with anti-CD122 treatment. Differential gene expression was compared among the subset of genes identified to be differentially induced in memory P14 cells following bystander PV infection compared to naive cells. (D) Expression level of the 44 genes identified to belong to the “cell cycle” GO term by DAVID analysis in memory P14 cells exposed to bystander PV infection compared to memory P14 cells exposed to bystander PV infection combined with anti-CD122 treatment. Data in (A) are from 3 mice per group, representative of 3 independent experiments and analyzed by two-tailed, unpaired Student’s t-test. Data in (B, C) are from 3 independent RNA pools per group collected from at least 2 mice per pool ($1x10^6$ purified memory P14 cells per pool).



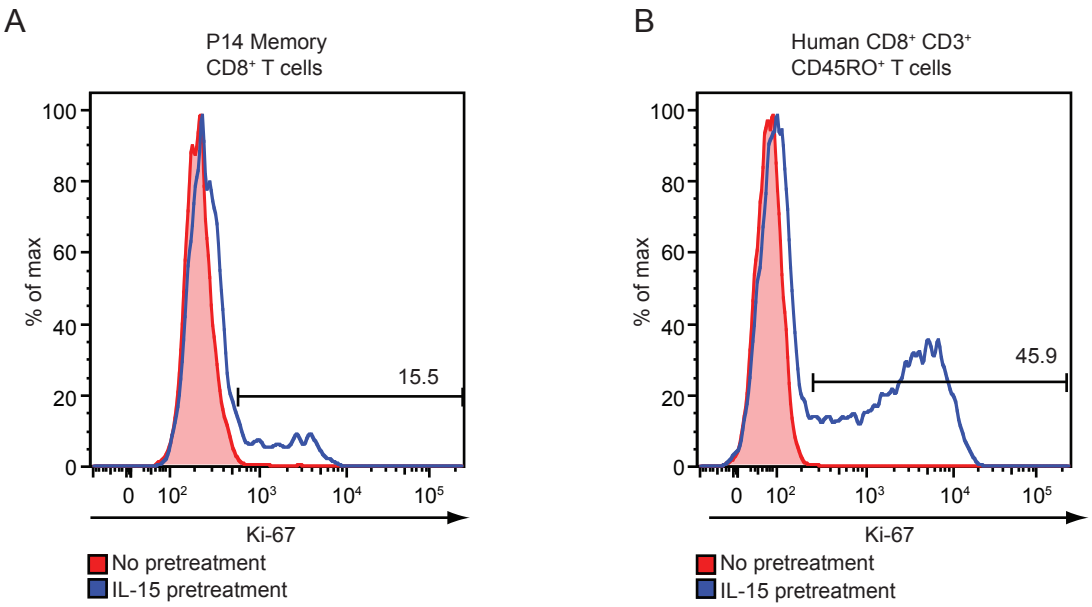
Supplemental Figure 4 : IL-2 does not regulate cell cycle entry of memory CD8⁺ T cells following bystander viral infection. (A) Representative plots of Ki-67 expression by memory P14 cells on day 4 following mock-infection or infection with PV followed by daily treatment with either Rat IgG or anti-IL-2 (clone JES6-1A12) antibody as indicated. Shaded histograms are isotype controls. (B) Cumulative data (mean ± SEM) of Ki-67 expression by memory P14 cells on day 4 following indicated treatment. Data are from 3 mice per group and representative of 2 independent experiments. Data in (B) were analyzed by One-way ANOVA with Tukey's post-test of multiple comparisons.



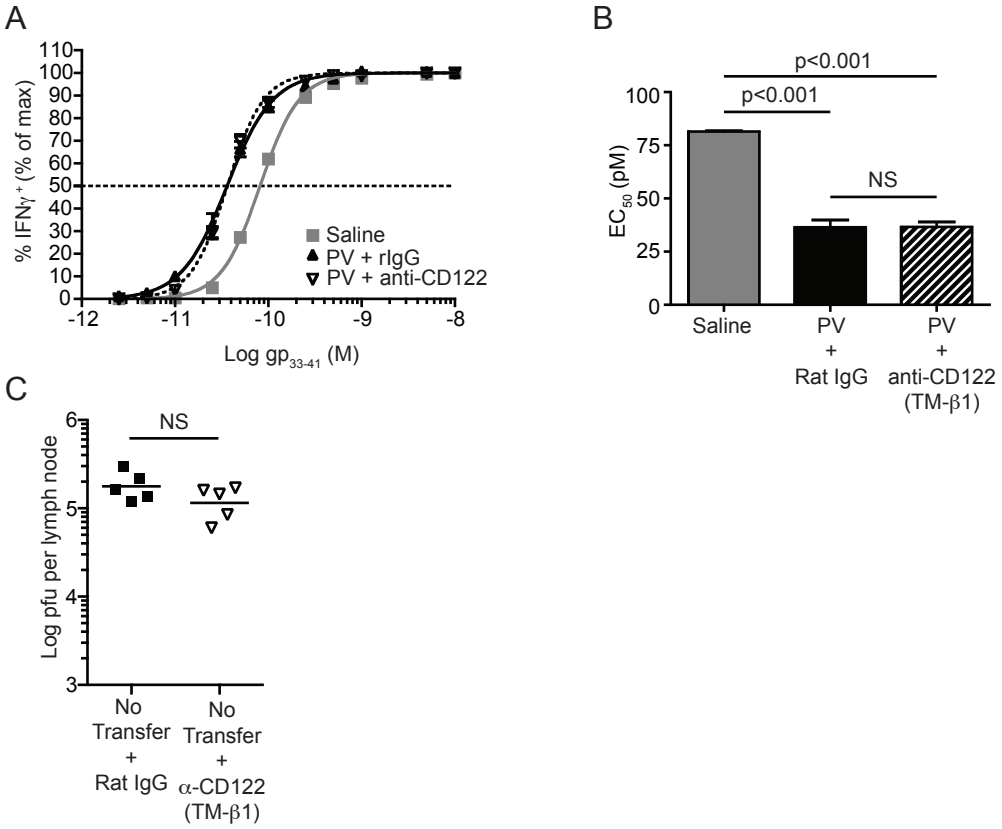
Supplemental Figure 5 : Viral infection induces upregulation of CD215 on dendritic cells.
(A) Representative plots of CD215 expression by dendritic cells (CD11c^{hi} MHC classII^{hi}) on day 2 following infection with PV or mock-infection with saline as indicated. Shaded histograms are isotype controls (B) Cumulative data (mean ± SEM) of geometric mean fluorescence intensity (gMFI) of CD215 expression by dendritic cells on day 2 following indicated treatment. (C, D) Same as (A, B) for macrophages/monocytes (F4/80^{+} CD11b^{+}). (E, F) Same as (A, B) for B cells (CD19^{+} Thy1.2^{-}) Data are from 3 mice per group and representative of 3 independent experiments. Data in (B, D, F) were analyzed by two-tailed unpaired Student's t-test.



Supplemental Figure 6: Signaling via the mTOR complex-1 is not required for upregulation of granzyme B by memory CD8⁺ T cells. (A) Representative plots of granzyme B expression by memory P14 cells on day 4 following indicated treatment. Gray shaded histograms represent isotype controls. (B) Cumulative data (mean ± SEM) geometric mean fluorescence intensity (gMFI) of granzyme B expression by memory P14 cells on day 4 following indicated treatment. Data are from 3 mice per group and representative of at least 2 independent experiments. Data in (B) were analyzed by One-way ANOVA with Tukey's post-test of multiple comparisons.



Supplemental Figure 7: Pre-treatment with low dose IL-15 induces ki-67 expression and leads to faster proliferation following TCR triggering. (A) Representative plots of Ki-67 expression by memory P14 cells 4 days with (blue line) or without (red shaded histogram) pre-treatment with recombinant IL-15. (B) Same as (A) for human antigen experienced $CD8^+$ T cells. Data in (A) is from $CD8^+$ T cells purified from at least 3 pooled mice and representative of 2 independent experiments. Data in (B) is from one human donor and representative of 2 independent experiments.



Supplemental Figure 8: IL-15 signaling does not regulate the antigen sensitivity of memory CD8⁺ T cells following bystander viral infection. (A) % IFN-γ⁺ memory P14 cells at day 4 after mock-infection with saline (grey line) or infection with PV and daily treatment with Rat IgG (black line) or anti-CD122 (clone TM-β1) (dashed black lines) determined after ex vivo stimulation with titrated concentrations of gp_{33-41} peptide. Data (mean ± SEM) are normalized to % IFN-γ+ cells at peptide saturation (10nM). (B) Cumulative data (mean ± SEM) of effective concentration $(EC)_{50}$ for stimulation of IFN-γ production by memory P14 cells. (C) Viral burden in the inguinal lymph node on day 3 following infection with LCMV clone 13 infection of mice receiving no memory CD8⁺ T cells and treated daily with either Rat IgG (black squares) or anti-CD122 (clone TM-β1) (open inverted triangles. Data in (A, B) are from 3 mice per group, representative of 2 independent experiments. Data in (B) were analyzed by One-way ANOVA with Tukey's post-test of multiple comparisons.
Data in (C) are from 5 mice per group, representative of 2 independent experiments and analyzed by two-tailed unpaired Student's t-test.

Supplemental Table 1: DAVID analysis of differentially regulated genes in memory P14 T cells following Pichinde virus infection with or without treatment with anti-CD122.

GO TERM (top 5)	# of genes	p value
cell cycle	44	5.20E-45
M phase	35	7.80E-40
cell cycle process	37	2.00E-38
M phase of the mitotic cell cycle	31	3.50E-38
cell cycle phase	35	5.80E-38

Supplemental Table 2: Proliferation index of memory CD8 T cells following pretreatment with or without IL-15 and TCR triggering

Proliferation Index

		Experiment #1		Experiment #2	
	Days	No Pretreatment	IL-15 Pretreatment	No Pretreatment	IL-15 Pretreatment
P14 Memory $CD8^+$ T cells	0	1	1	1.19	1.16
	1	1	1.23	1.17	1.23
	2	1.22	1.34	1.27	1.64
	3	1.95	2.1	1.94	2.15
Human $CD8^+$ $CD3^+$ $CD45RO^+$ T cells	0	1	1	1	1
	1	1	1.09	1.74	1.91
	2	1.03	1.54	1.84	2.03
	3	1.83	2.28	2.42	3.06