Supplemental Figure Legends

Supplemental Figure 1. Aging elevates production of TNF-α during HSV-2 infection. p =0.002 (ANOVA). Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 2. Age-dependent increases in HSV-2-induced IL-17A production and mortality in the BALB/c, H2^{d} mouse strain. Values in A represent the mean+/-SD of two independent experiments each performed in triplicate. Significant differences were noted in IL-17A production (p <0.001, ANOVA) and mortality (p = 0.01, Logrank).

Supplemental Figure 3. Aged BALB/c mice succumb to MCMV infection and exhibit elevated IL-6, IL-17A, and TNF-α serum levels, whereas young counterparts survive with lower proinflammatory cytokine responses. Values in A-C represent the mean+/-SD of two independent experiments each performed in triplicate. Young and aged mice exhibited significantly different cytokine levels (p < 0.001, ANOVA) and survival (p = 0.01, Logrank).

Supplemental Figure 4. Aged HSV-2-infected C57BL/6 mice exhibit a dose-dependent elevation in serum IL-17A levels as well as impaired IFN-α responses and viral clearance. Effect of HSV-2 infection on serum IL-17A levels (A), serum

IFN-α levels (B), and serum viral load (C) in young and aged mice. Viral load was measured using the plaque assay. Values in A-C represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 5. A dose of 10^7 PFU of HSV-2 is lethal to aged C57BL/6 mice and induces greater cytokine production than sub-lethal infection with 10^5 PFU HSV-2. Comparison of 10^7 PFU and 10^5 PFU of HSV-2 on serum levels of IL-6 (A), IL-17A (B) and TNF-α (C) as well as mortality (D). Values in A-C represent the mean+/-SD of two independent experiments each performed in triplicate. Levels of all three cytokines differed between each dose group ($p < 0.05$, ANOVA), as did mortality ($p = 0.01$, Logrank).

Supplemental Figure 6. Aged BALB/c mice exhibit higher levels of ALT during MCMV infection than their young counterparts. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 7. A dose of 10^7 PFU of HSV-2 induces higher serum ALT levels than 10^5 PFU of HSV-2 in aged C57BL/6 mice. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 8. Nine-month-old BALB/c Jα18$^{-/-}$ mice exhibit lower serum IL-17A levels during HSV-2 infection than their age-matched wild type

counterparts. Values represent the mean+/-SD of two independent experiments each performed in triplicate. $p = 0.01$ (ANOVA) between the two groups.

Supplemental Figure 9. Aged mice exhibit a greater number of liver NKT cells than young mice prior to infection. Infection did not alter the number of NKT cells in either group. Values represent the mean+/-SD of two independent experiments each performed in triplicate.* $p = 0.03$ (T-test)

Supplemental Figure 10. Middle-aged wild type and IL-6$^{-/-}$ mice exhibit similar IL-17A levels during HSV-2 infection. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

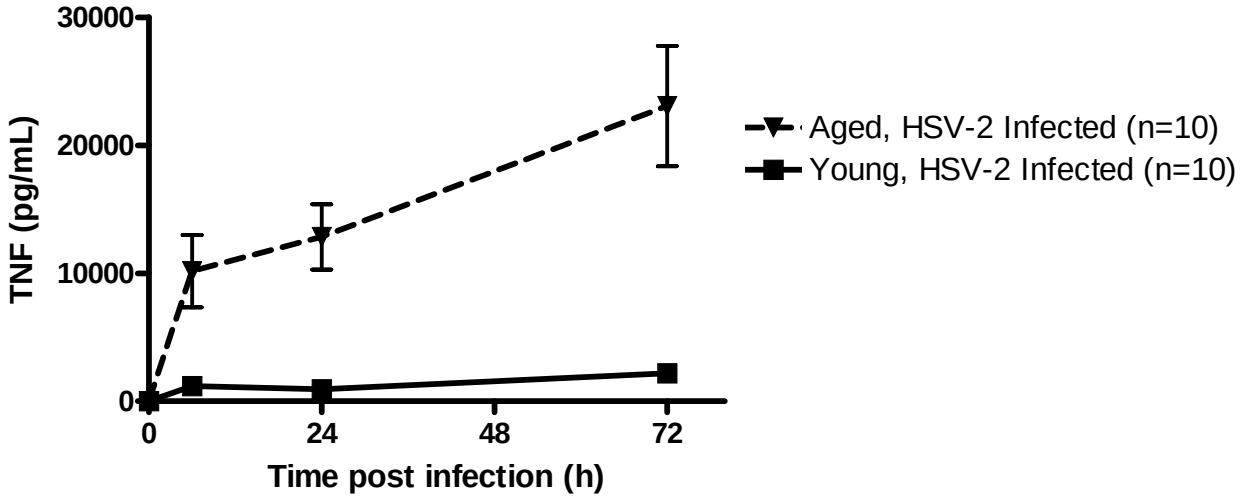
Supplemental Figure 11. Depletion of pDCs in young, HSV-2 infected C57BL/6 mice leads to increased viral load in the liver. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 12. Administration of recombinant IL-17A to non-infected young or aged mice does not induce serum ALT release at 24h post administration (A) despite inducing high serum IL-17A levels (B). All mice that received recombinant IL-17A remained clinically well without any mortality. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 13. HSV-2 viral load is comparable between aged mice treated with anti-IL-17A antibody and isotype control antibody as measured by plaque assay in liver and spleen (A) and viral load PCR assay in the serum (B). Values represent the mean+/-SD of two independent experiments each performed in triplicate.

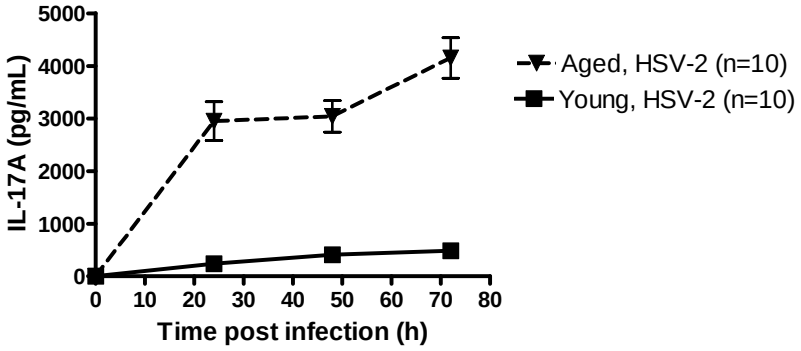
Supplemental Figure 14. Anti-IL-17A antibody treatment reduces serum TNF-α levels 24 h after HSV-2 infection in aged mice. Values represent the mean+/-SD of two independent experiments each performed in triplicate.

Supplemental Figure 15. IL-17A neutralization decreases ALT levels and mortality in aged mice infected with MCMV or HSV-2. (**A, B**) Effect of α-IL-17A neutralizing antibody or an isotype control on ALT levels (A) and survival (B) in BALB/c mice following MCMV infection. (**C, D**) Effect of α-IL-17A neutralizing antibody or an isotype control on ALT levels (C) and survival (D) in C57BL/6 mice at 24 h after HSV-2 infection. IL-17A neutralization significantly enhanced survival in both MCMV-infected BALB/c mice and HSV-infected C57BL/6 mice ($p = 0.02$ for both, Logrank). Values in A and C represent the mean+/-SD of two independent experiments each performed in triplicate.



Supplemental Figure 1

A



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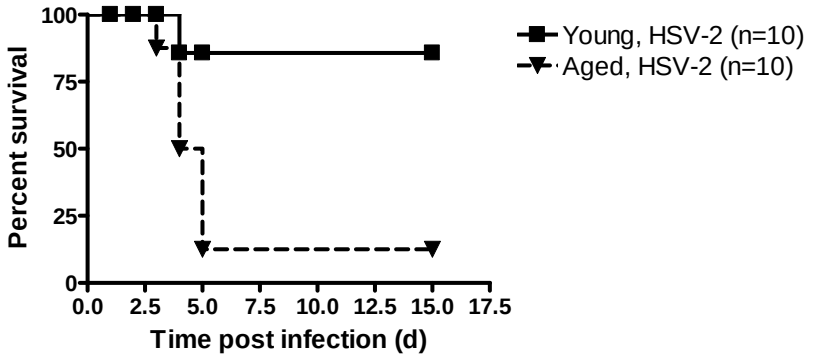

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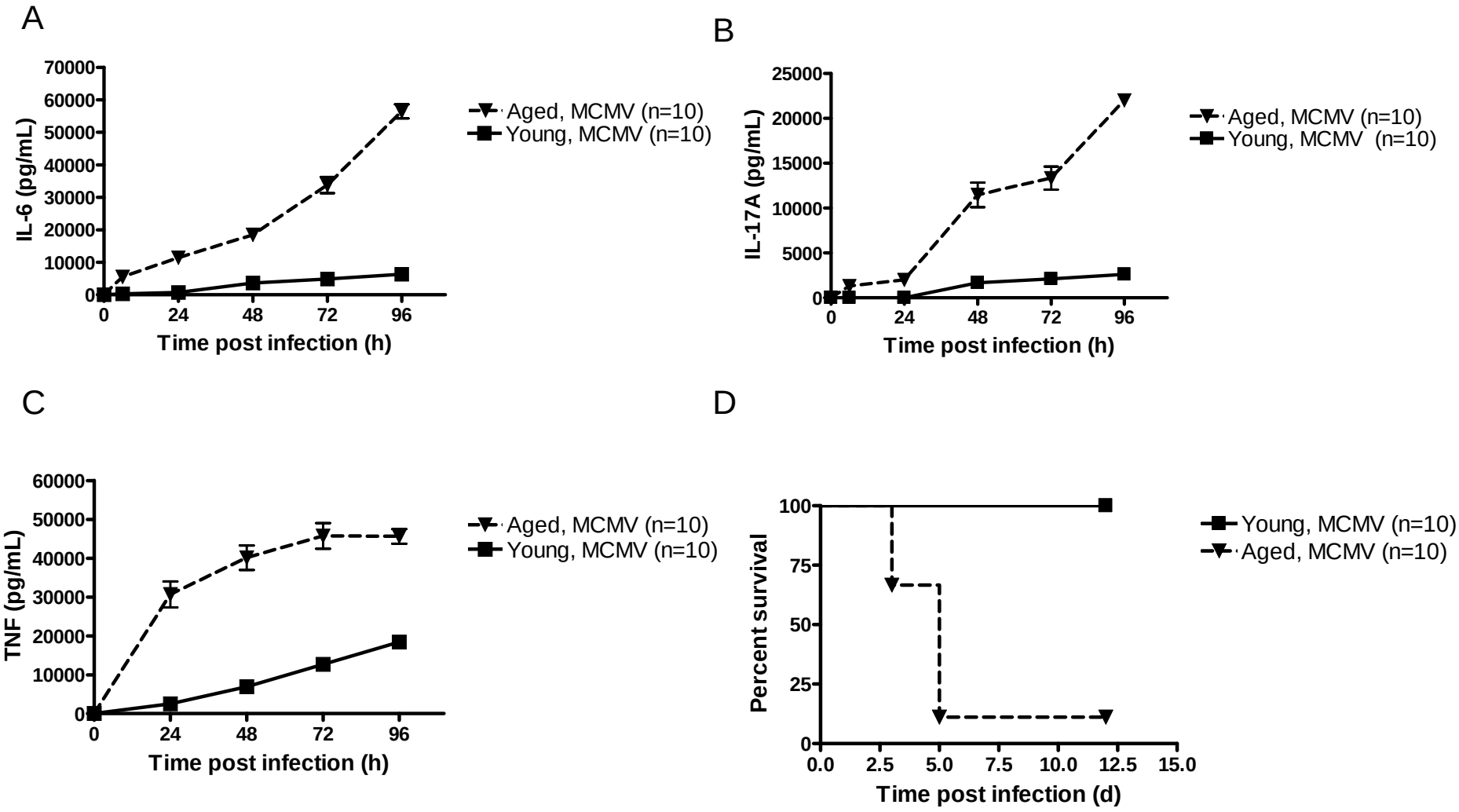

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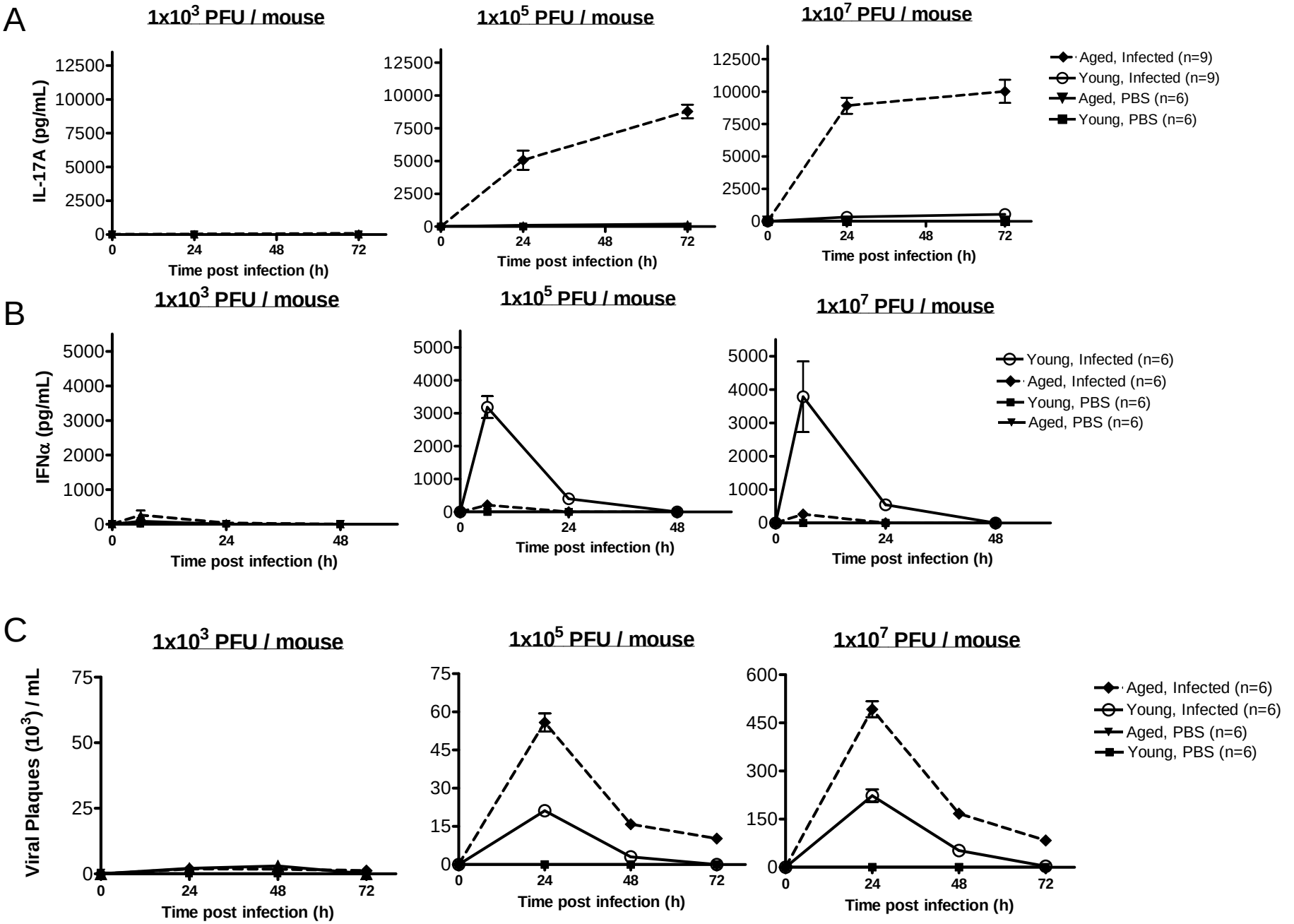

Supplemental Figure 4

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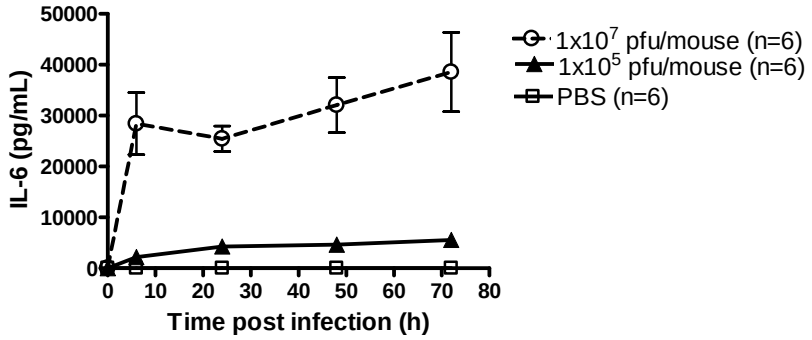

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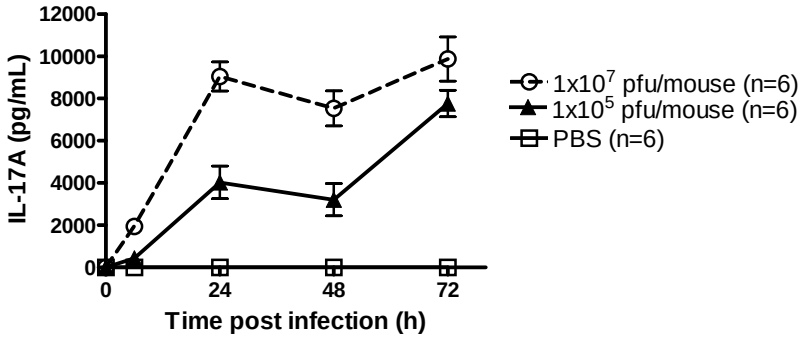

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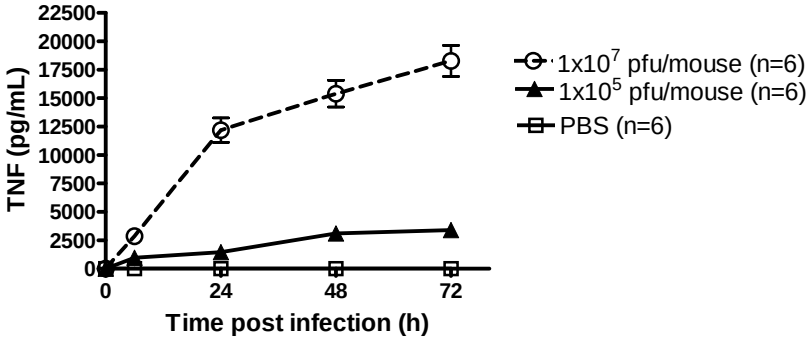

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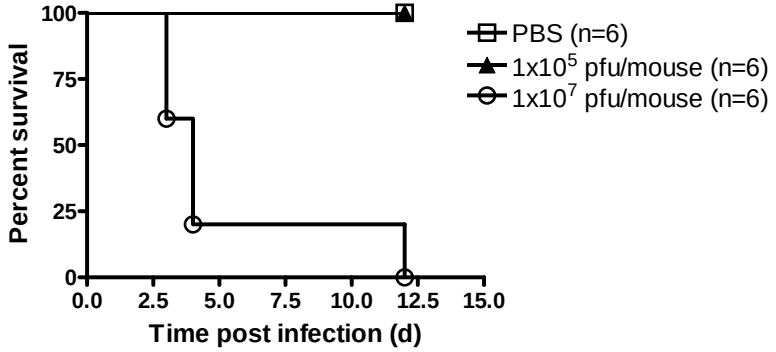

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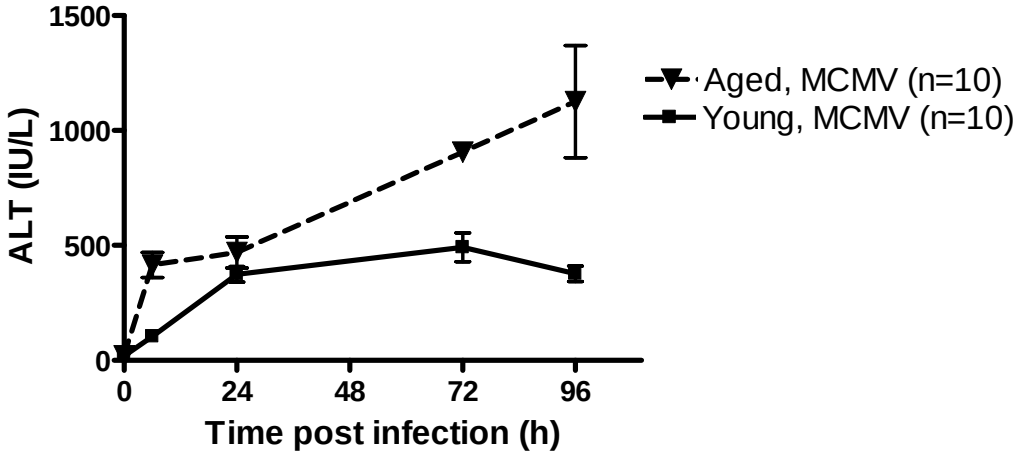

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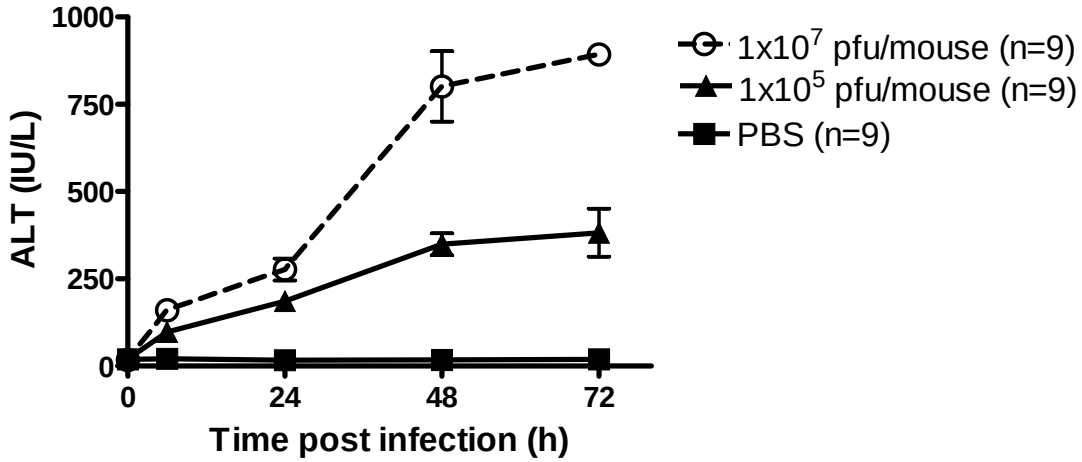

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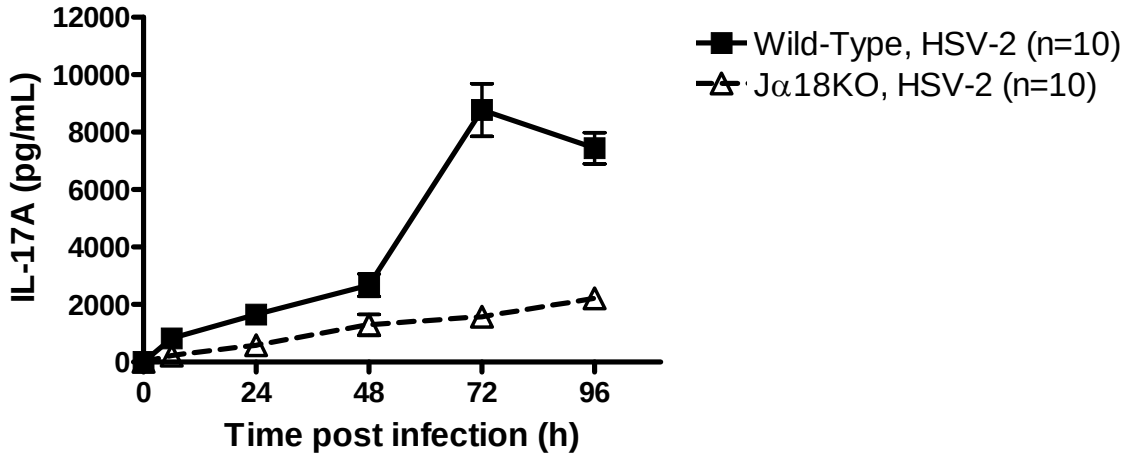

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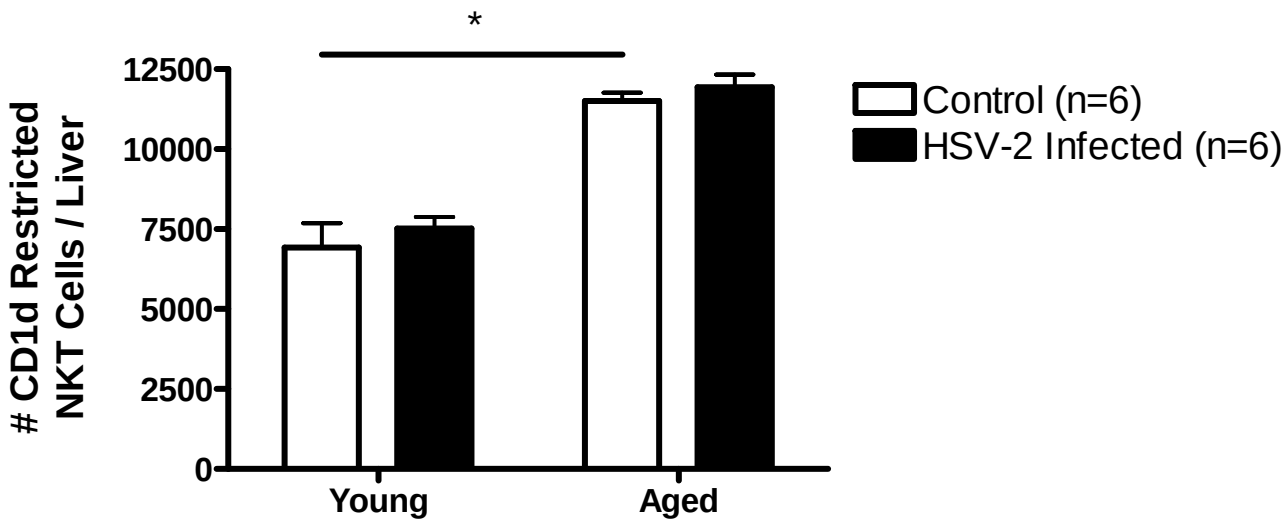

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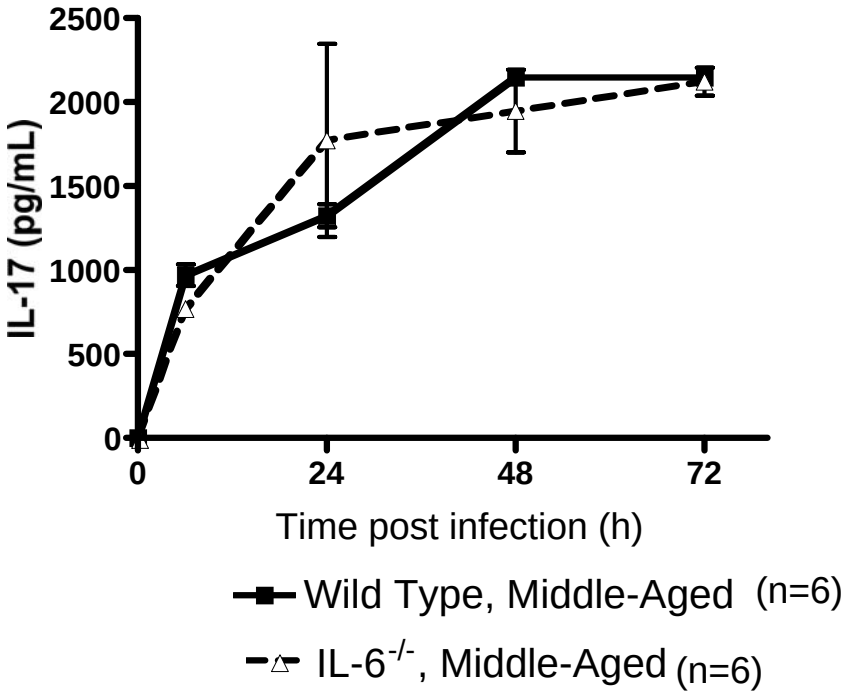

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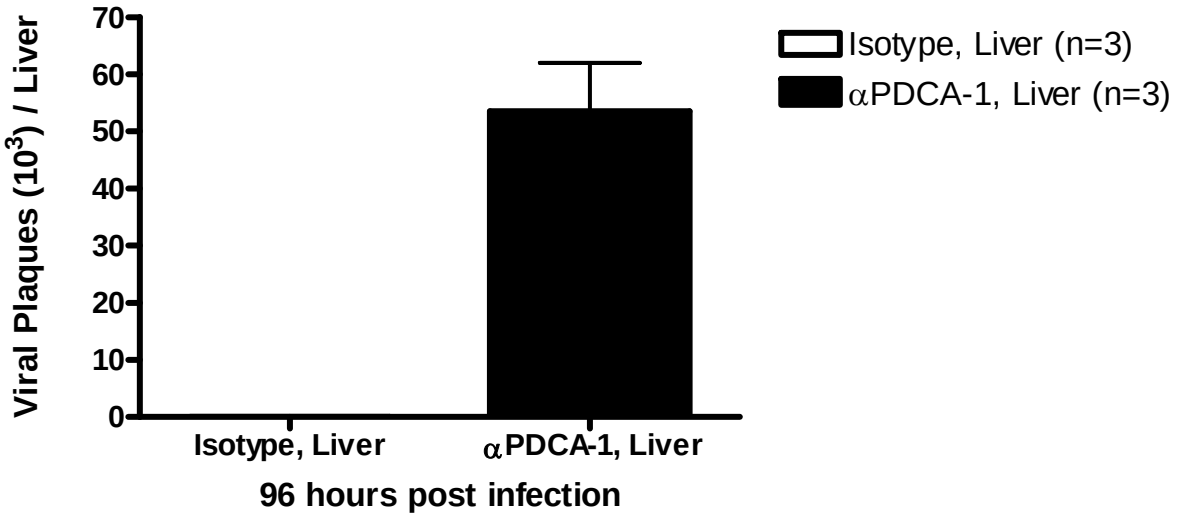

Supplemental Figure 11

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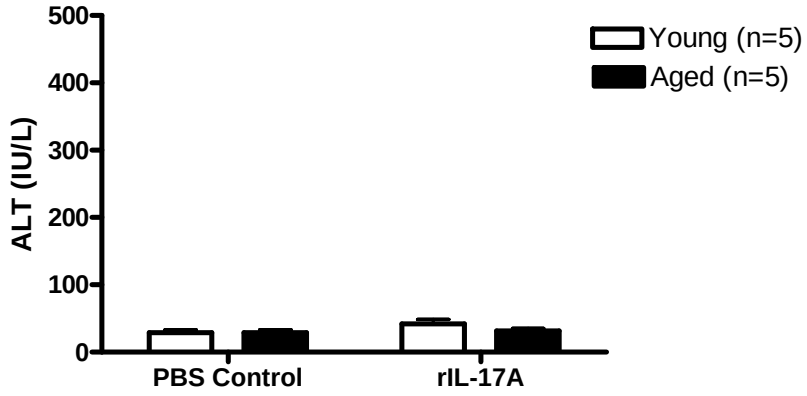

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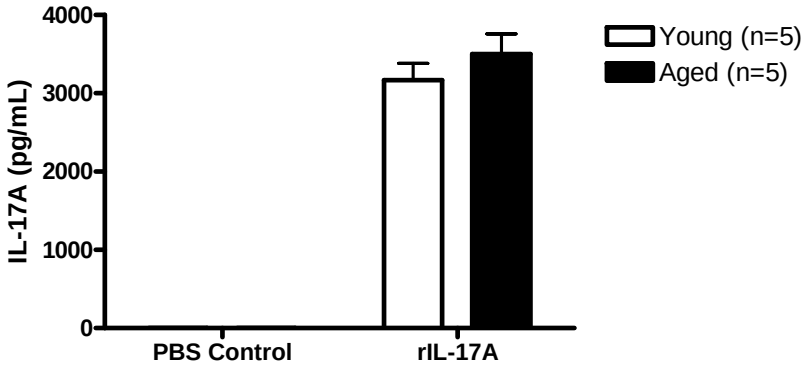

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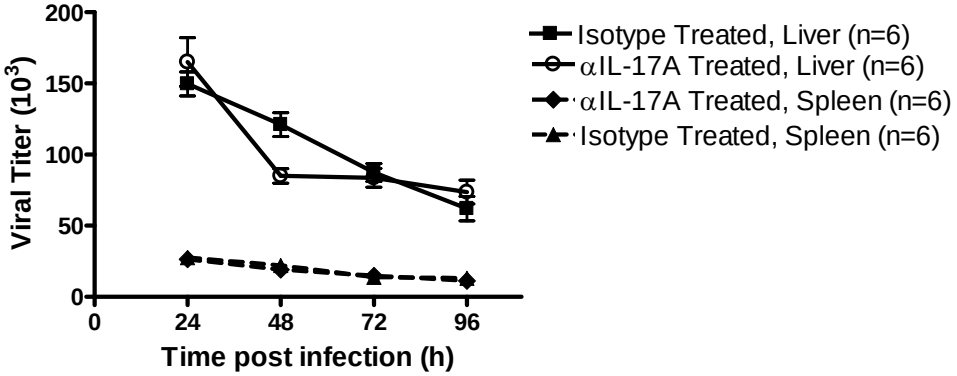

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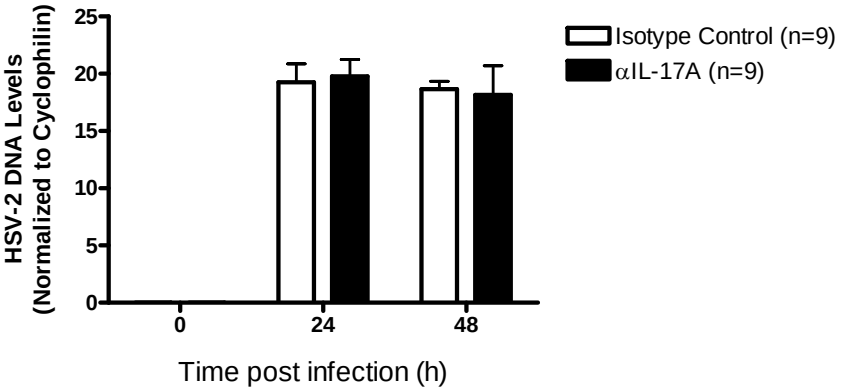

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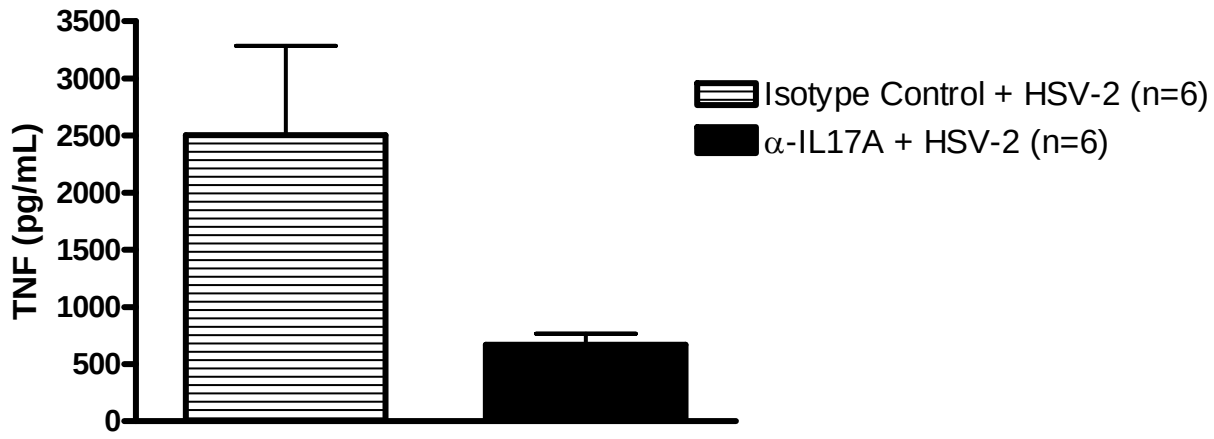

Supplemental Figure 14

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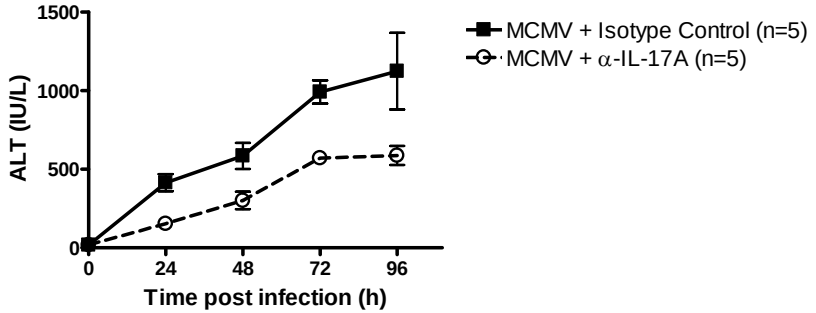

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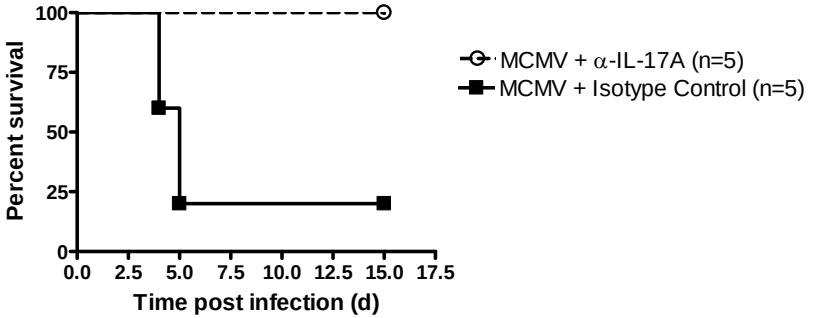

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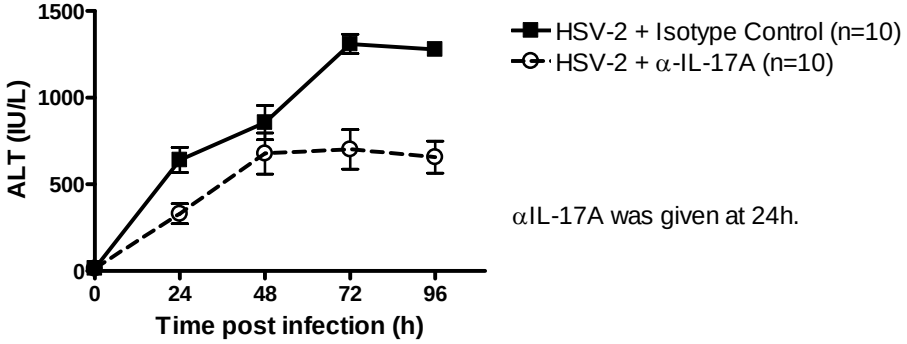

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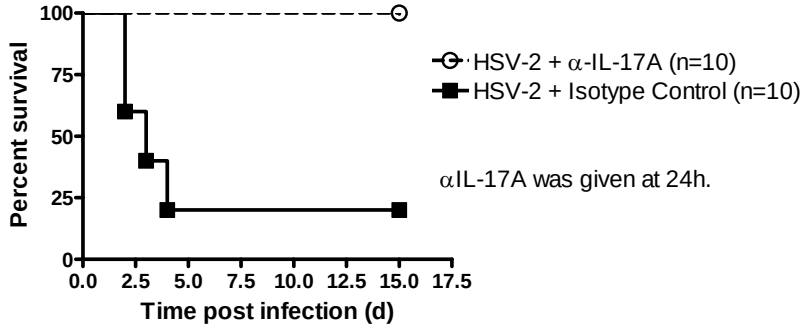

Supplemental Figure 15