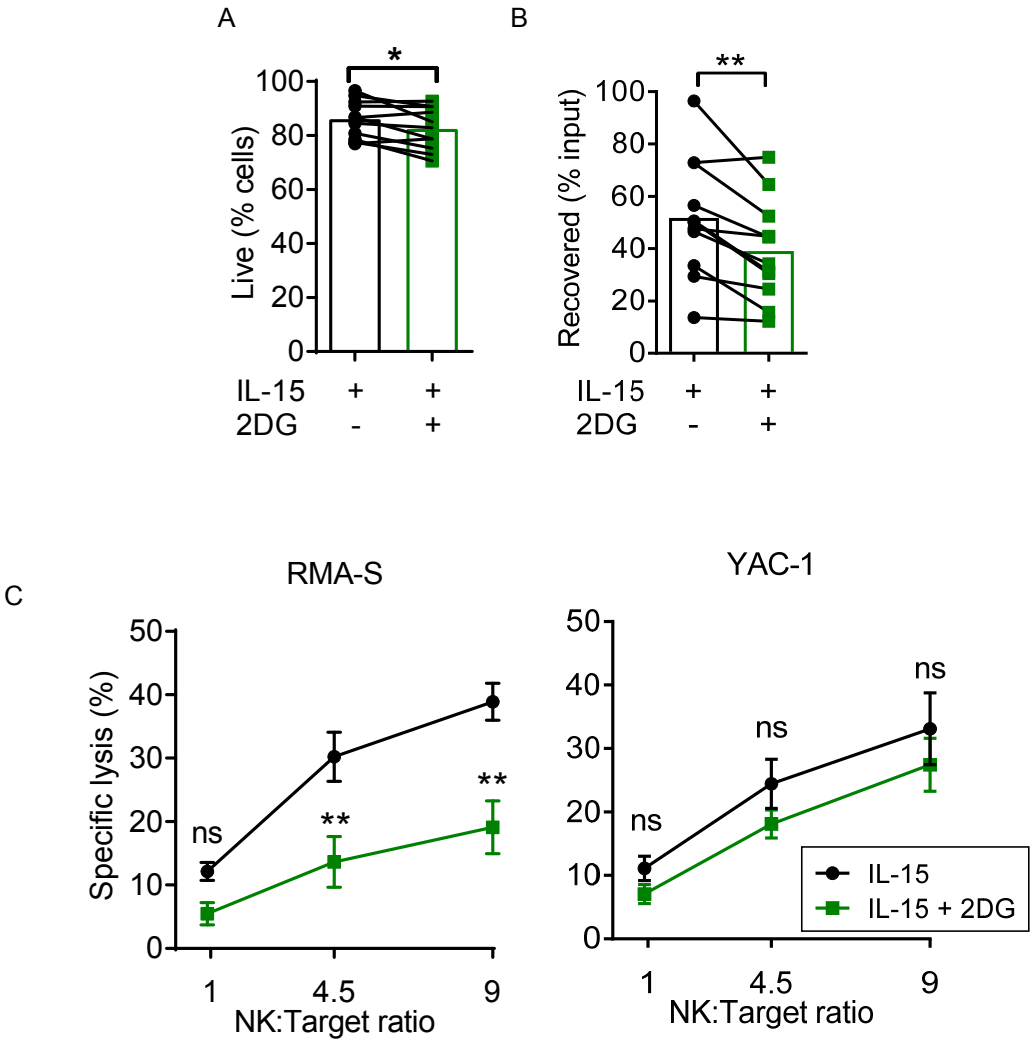
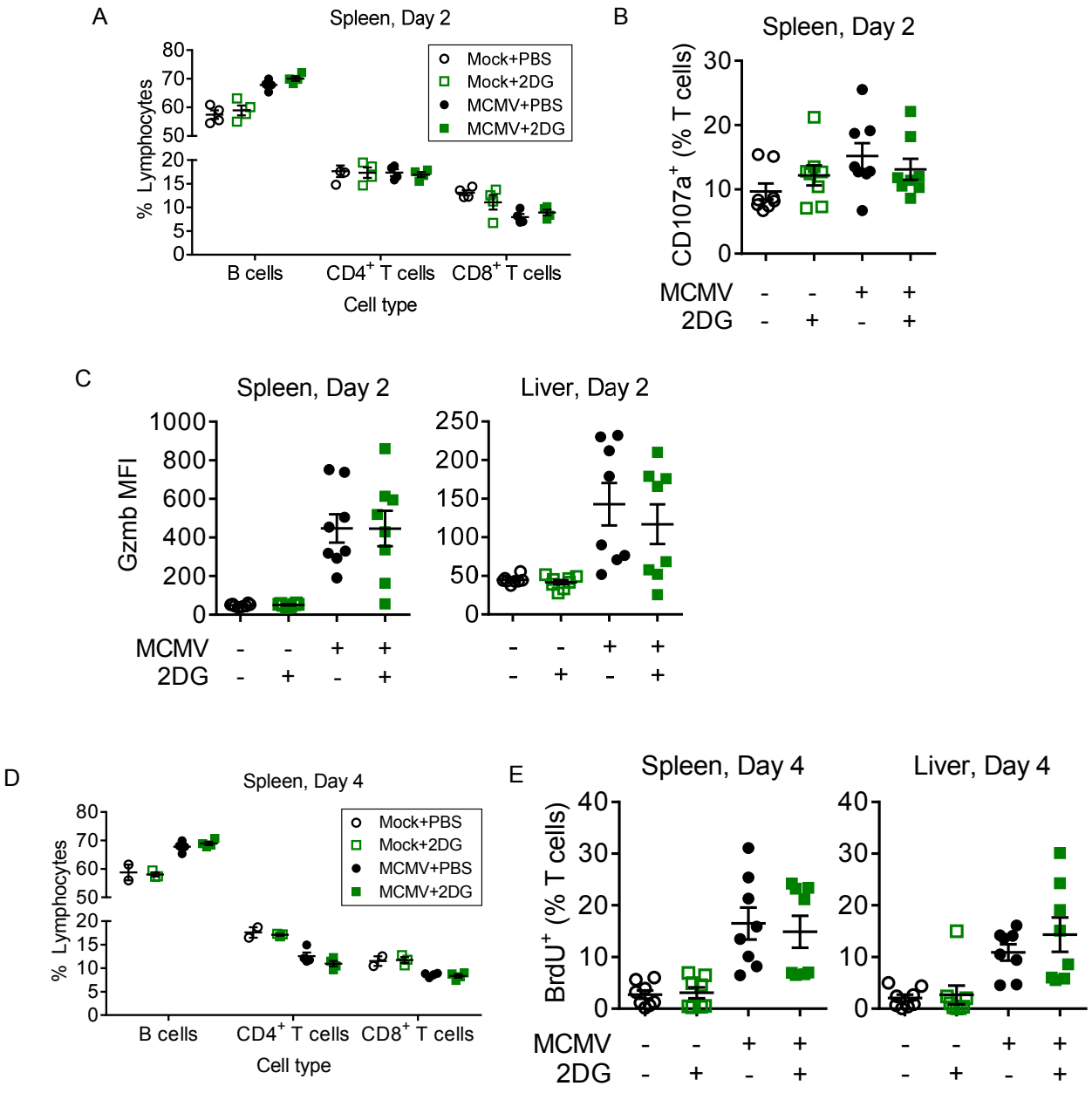
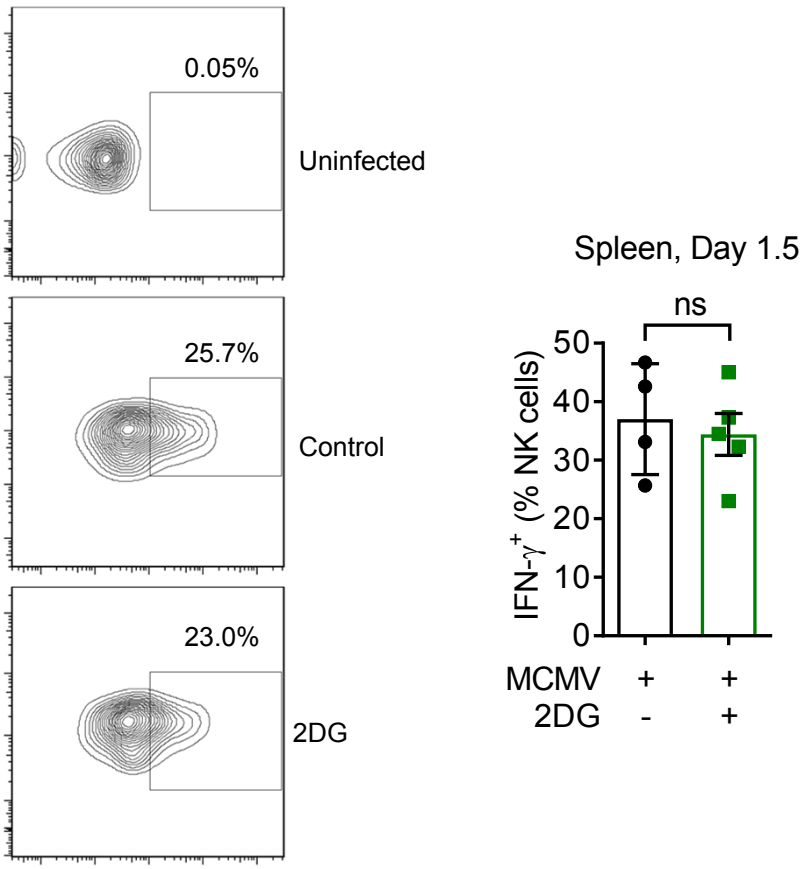


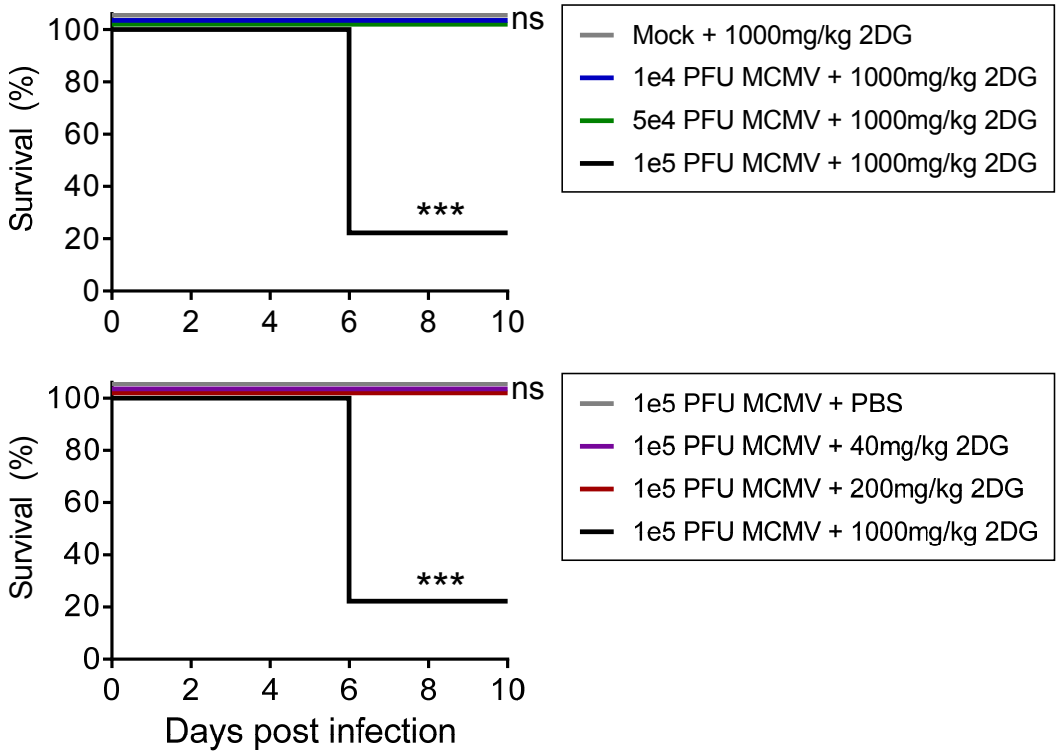
Supplementary Figure 1. Effects of 1mM 2DG culture on NK cell metabolism and killing. Purified NK cells were cultured in 100ng/mL IL-15 with 1mM 2-deoxy-D-glucose (2DG) for 72 hours. A) Percentage of cells alive by trypan blue staining and B) percentage of NK cells recovered after 72-hour culture out of total number of NK cells plated (n=11 individuals, 7 separate experiments, paired t test). C) Specific lysis of RMA-S and YAC-1 target cells after culture with IL-15-activated NK cells that had been cultured in normal media (black) or 1mM 2DG (green) (n=4 individuals, 1 experiment, 2-way ANOVA, mean +/- SEM). ns = not significant ($p \geq 0.05$), **=$p < 0.01$.



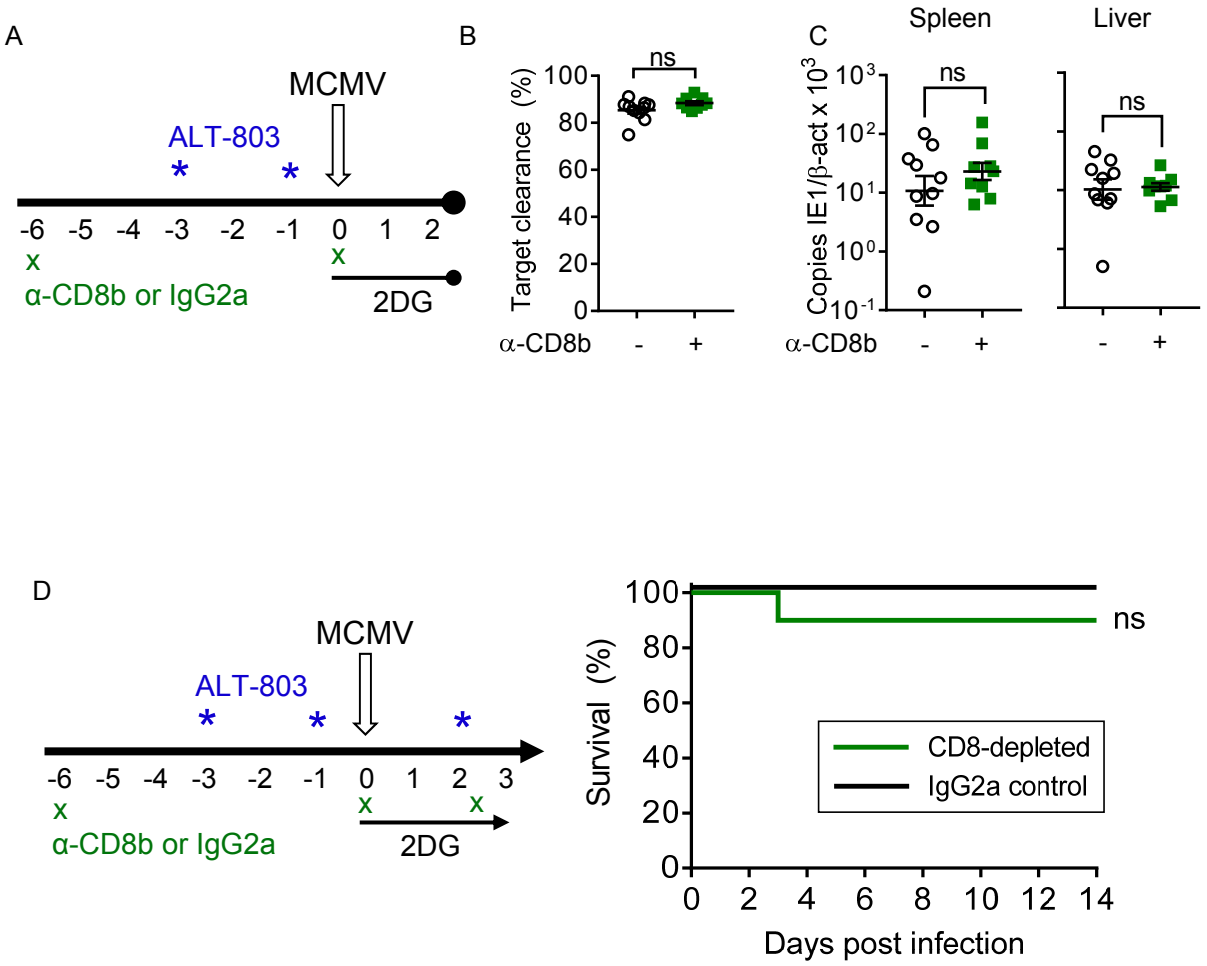
Supplementary Figure 2. T cells upregulate Gzmb and proliferate, but are not affected by 2DG treatment. The mice from Figure 4,C57BL/6 females infected with 1 x 10^5 PFU murine cytomegalovirus (MCMV) and treated with 1g/kg 2-deoxy-D-glucose (2DG) daily, were assessed for T cell function. A) The proportion of $CD19^+$ B cells, $CD3^+CD4^+$ T cells, and $CD3^+CD8^+$ T cells in the spleen at day 2 post-infection (n=4/group, representative of 2 experiments). $CD3^+NK1.1^-$ cells were assessed using flow cytometry for (B) degranulation by CD107a staining directly ex vivo and (C) granzyme B expression as mean fluorescence intensity (Gzmb MFI). D) Proportion of $CD19^+$ B cells, $CD3^+CD4^+$ T cells, and $CD3^+CD8^+$ T cells in the spleen at day 4 post-infection (n=3-4/group, representative of 2 experiments). C) BrdU incorporation 3 hours after injection (n=7-8 individuals/group, 2 experiments) on day 4 post-infection. Data show mean +/- SEM, no significant differences were found between control and 2DG groups by 1-way ANOVA ($p \geq 0.05$).



Supplementary Figure 3. **IFN-γ production by NK cells during MCMV infection is not inhibited by 2DG.** Mice were infected with 1 x 10^5 PFU murine cytomegalovirus (MCMV) and injected with 1g/kg 2-deoxy-D-glucose (2DG) or PBS. Mice were sacked at 36 hours post-infection for flow cytometry (n=4-5 individuals/group, 2 separate experiments). Data show mean +/- SEM, ns = not significant ($p \geq 0.05$).



Supplementary Figure 4. MCMV susceptibility is dependent on the dose of 2DG and the inoculum of MCMV. 8-week-old female C57BL/6 mice were infected with murine cytomegalovirus (MCMV) and injected daily with 2-deoxy-D-glucose (2DG). Either the MCMV inoculum or 2DG dosage was varied. Survival is shown for 10 days, with the same mice for 1 x 10^5 pfu MCMV + 1000mg/kg 2DG (black) shown in both graphs (n=5/group, 1 experiment, log-rank Mantel Cox Test). ns = not significant ($p \geq 0.05$), *** = $p < 0.001$.



Supplementary Figure 5. The effects of ALT-803 are not mediated through CD8⁺ T cells. A) Mice were depleted of CD8⁺ T cells using α-CD8b, or were treated with IgG2a as a control. Mice were then given two doses of 5μg ALT-803, infected with 1 x 10^5 PFU murine cytomegalovirus (MCMV), and injected with 1g/kg 2-deoxy-D-glucose (2DG) daily. B) Clearance of *m157*-transgenic targets from the spleen and (C) copy number of MCMV in the spleen and liver were assessed on day 2 (n=9-10 individuals/group, 1 experiment, copy number data log-transformed, analysis by t test). D) Mice were given an additional dose of ALT-803 and either α-CD8b (green, n=10) or IgG2a (black, n=5), and followed for 14 days (1 experiment, log-rank Mantel-Cox test). Data show mean +/- SEM or survival, ns=not significant (p≥0.05).