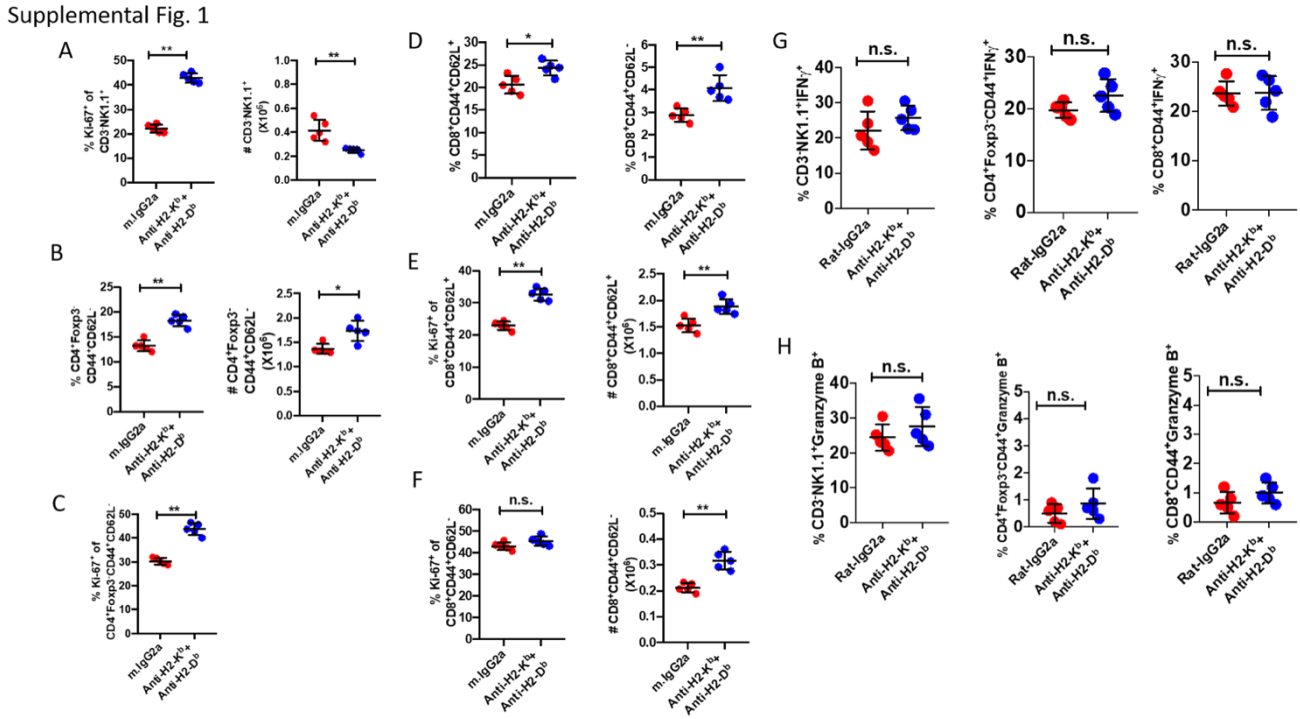
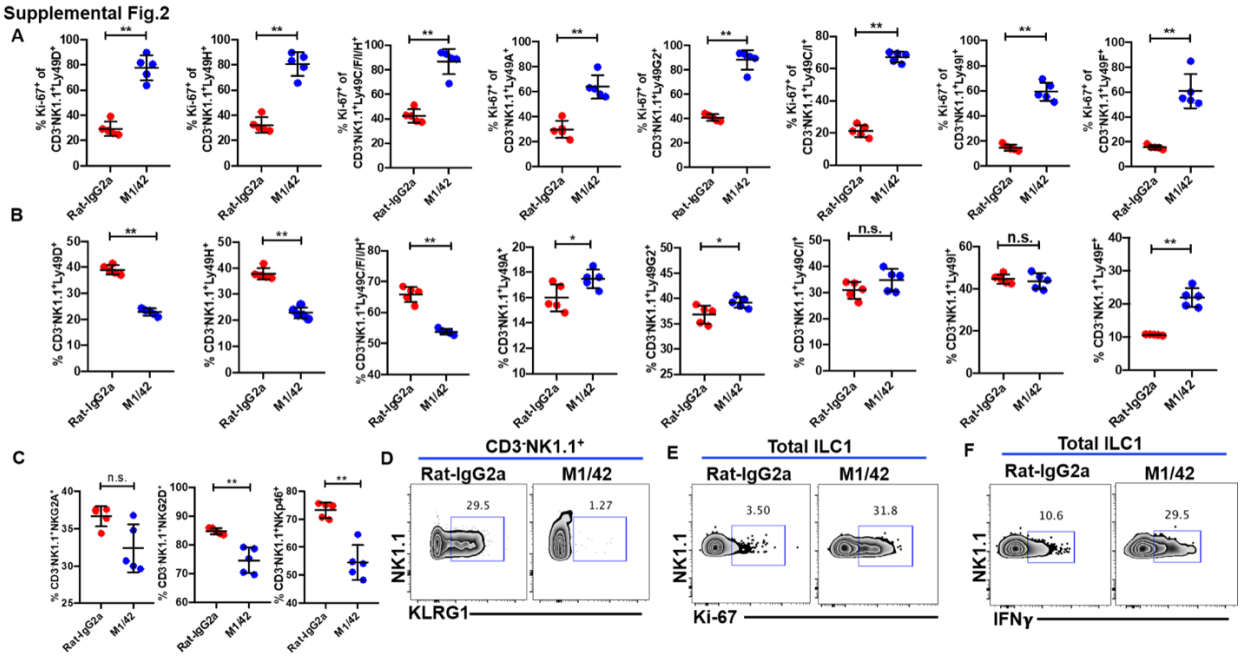
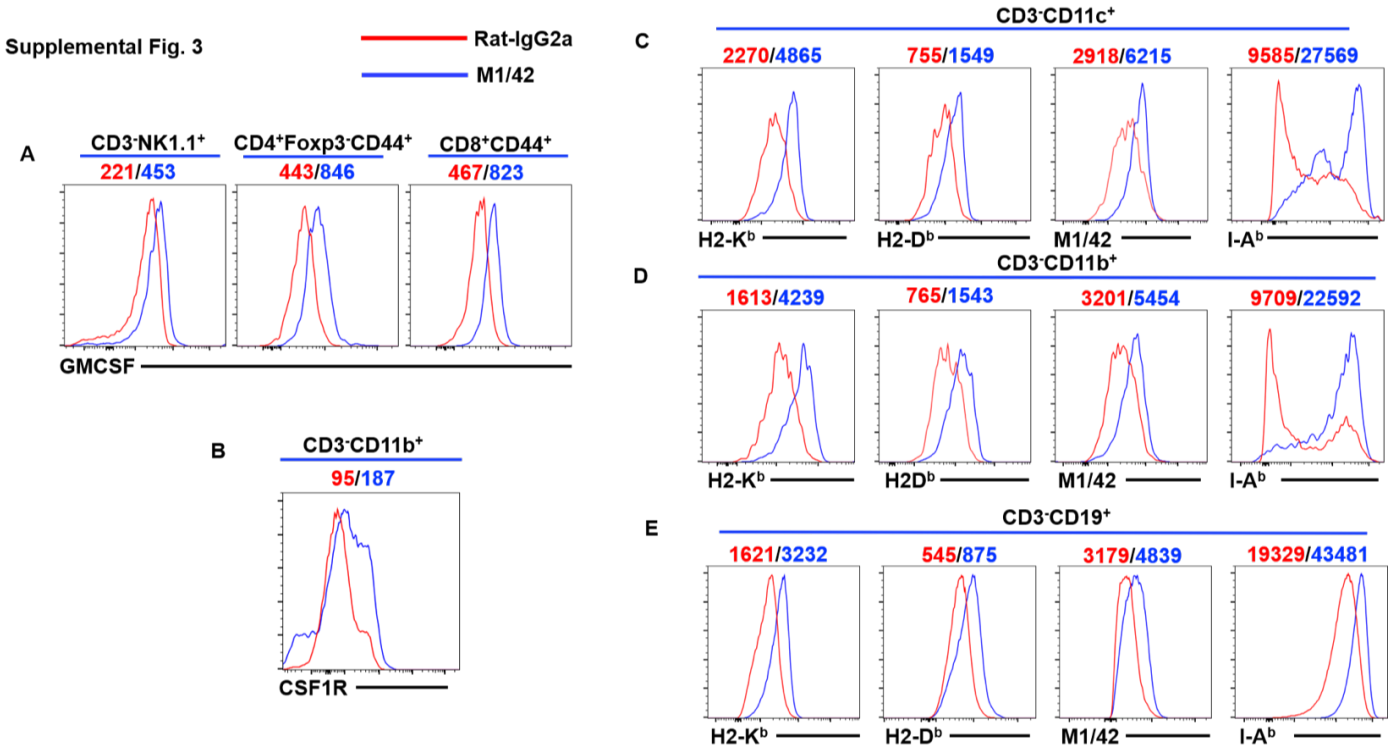



**Supplemental Figure 1**. Anti-H2-K$^{b}$ and anti-H2-D$^{b}$ co-treatment marginally enhanced NK cell and T cell proliferation. (A) Ki-67 expression and total number of CD3$^{-}$NK1.1$^{+}$ splenocytes after 8 days of treatment with mixture of anti H2-K$^{b}$ (AF6-88.5) and H2-D$^{b}$ (28-14-8). (B) Relative frequency and total number of CD4$^{+}$Foxp3$^{-}$CD44$^{+}$CD62L$^{-}$cells. (C) Relative Ki-67 expression in CD4$^{+}$Foxp3$^{-}$ CD44$^{+}$CD62L$^{-}$ cells. (D) Relative frequency of CD8$^{+}$CD44$^{+}$CD62L$^{+}$ and CD8$^{+}$CD44$^{+}$CD62L$^{-}$ cells. (E &F) Relative Ki-67 expression and total no of CD8$^{+}$CD44$^{+}$CD62L$^{+}$ and CD8$^{+}$CD44$^{+}$CD62L$^{-}$ cells. (G &H) Relative cytokine production (IFN-γ and Granzyme B) from NK cells and MP T cells (CD4 and CD8) on day 8 after antibody co-treatment.

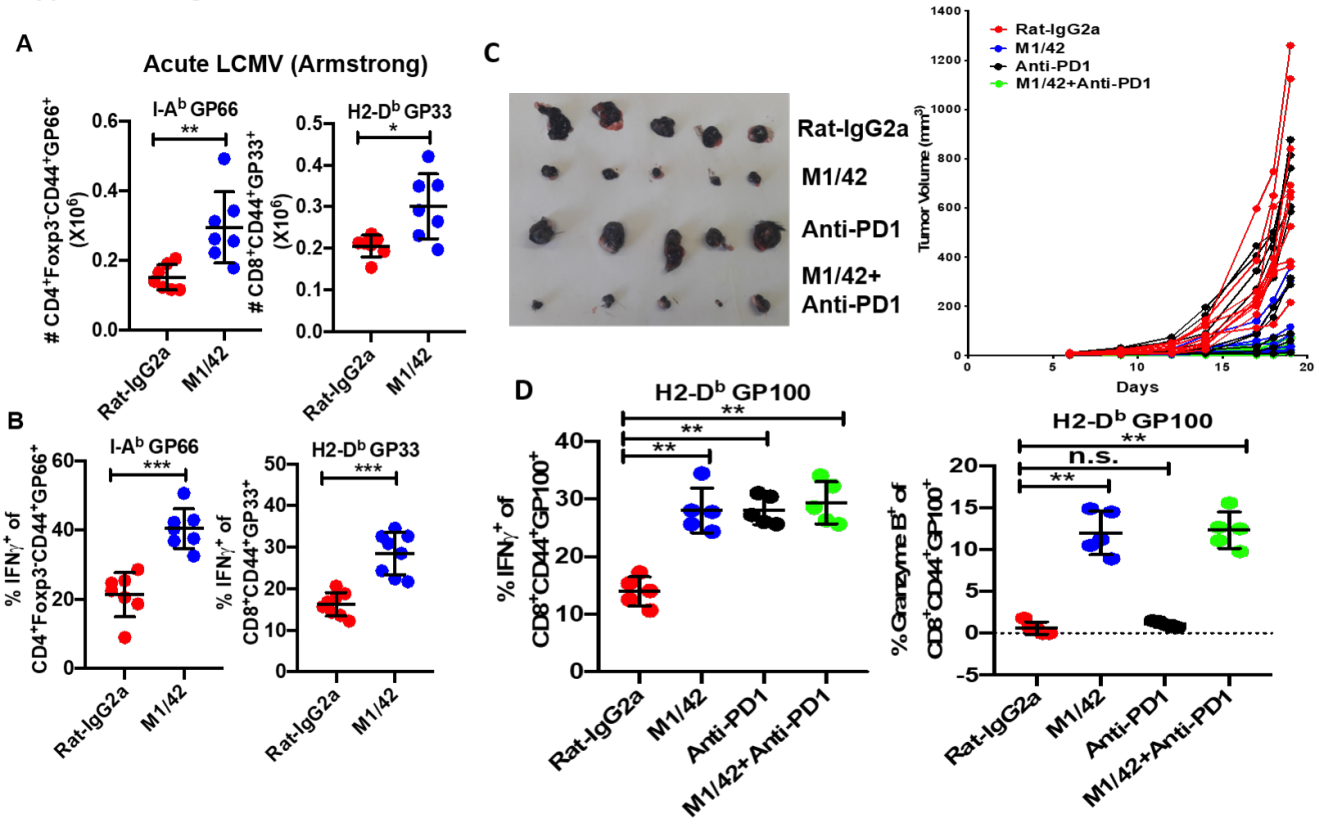



Supplemental Figure 2. M1/42 dramatically enhances NK cell activation in vivo.
(A) Percentage of NK cells expressing inhibitory receptors (Ly49A, Ly49C, LY49I, Ly49G2, Ly49F) and activation receptors (Ly49D and Ly49H) in splenocytes after M1/42 treatment. (B) Ki-67 expression of $CD3^{-}NK1.1^{+}Ly49^{+}$ (activation and inhibitory) gated NK cell subsets. (C) Surface expression of NKG2A, NKG2D and NKp46 on NK cells ($CD3^{-}NK1.1^{+}$) after M1/42 treatment. (D) Frequency of KLRG1 expression in on splenic NK cells after M1/42. (E) Ki67 expression and IFN-γ secretion by hepatic ILC1 after M1/42 treatment. The following clones were used: KLRG1 (2F1), NKp46 (29A1.4), NKG2D (1D11), NKG2A (16A11), Ly49A (A1/Ly49A or YE1/48.10.6), Ly49C/I (5E6), Ly49D (4E5), Ly49F (HBF-719), Ly49G2 (4D11), Ly49H (3D10), Ly49C/F/I/H (14B11). All antibodies were purchased from BD Biosciences. Liver ILC1 cells are define as: Live $CD45^{+}CD3^{-}NK1.1^{+}ROR\gamma t^{-}Gata3^{-}Tbet^{+}$ $CD49b^{-}$ $CD49a^{+}$.




**Supplemental Figure 3.** M1/42 activates GM-CSF production by NK cells and MP $CD4^+$ and $CD8^+$ T cells and enhanced expression of MHC-I and MHC-II on APC. C57BL/6 mice were treated with M1/42 or isotype control for six d and spleen cells were harvested on d 8. (A) Spleen cells were treated with PMA and ionomycin and GM-CSF production was measured by intracellular staining on gated NK cells, and MP $CD4^+$ and $CD8^+$ T cells. Results are expressed as Mean Fluorescence Intensity (MFI). (B) CSF1R expression (MFI) by monocytes ($CD3^-CD11b^+$) on day 8 after treatment. (C, D, E) MHC-I and MHC-II expression on monocytes ($CD3^-CD11b^+$), DC ($CD3^-CD11c^+$) and B cells($CD3^-CD19^+$) 8 days after M1/42 treatment.

Supplemental Fig. 4




**Supplemental Figure 4**. M1/42 enhances anti-viral and anti-tumor immunity. C57BL/6 mice were infected with LCMV Armstrong and treated with M1/42 (Day-2, 4, 7 and 10) and analyzed on d 15 (A) Total number of antigen-specific MP $CD4_+$ and $CD8_+$ T cells. (B) IFN-γ production by LCMV-specific MP $CD4^+$ and $CD8^+$ T cells after M1/42 treatment. (C) B16F10 tumor cells ($1.25 \times 10^5$) were injected s.c. Mice were treated with M1/42 (500μg/dose), anti-PD-1 (250μg /dose) or anti-PD-1 plus M1/42 every three d from d 3 to day 15. Tumor volume was determined. On d 17 tumor-bearing mice were sacrificed to analyze relative tumor size (left panel) and tumor volume (right panel). (D) Percentage of IFN-γ and Granzyme B producing tumor antigen-specific $CD8^+CD44^+GP100^+$ cells after M1/42 or anti-PD1 treatments.