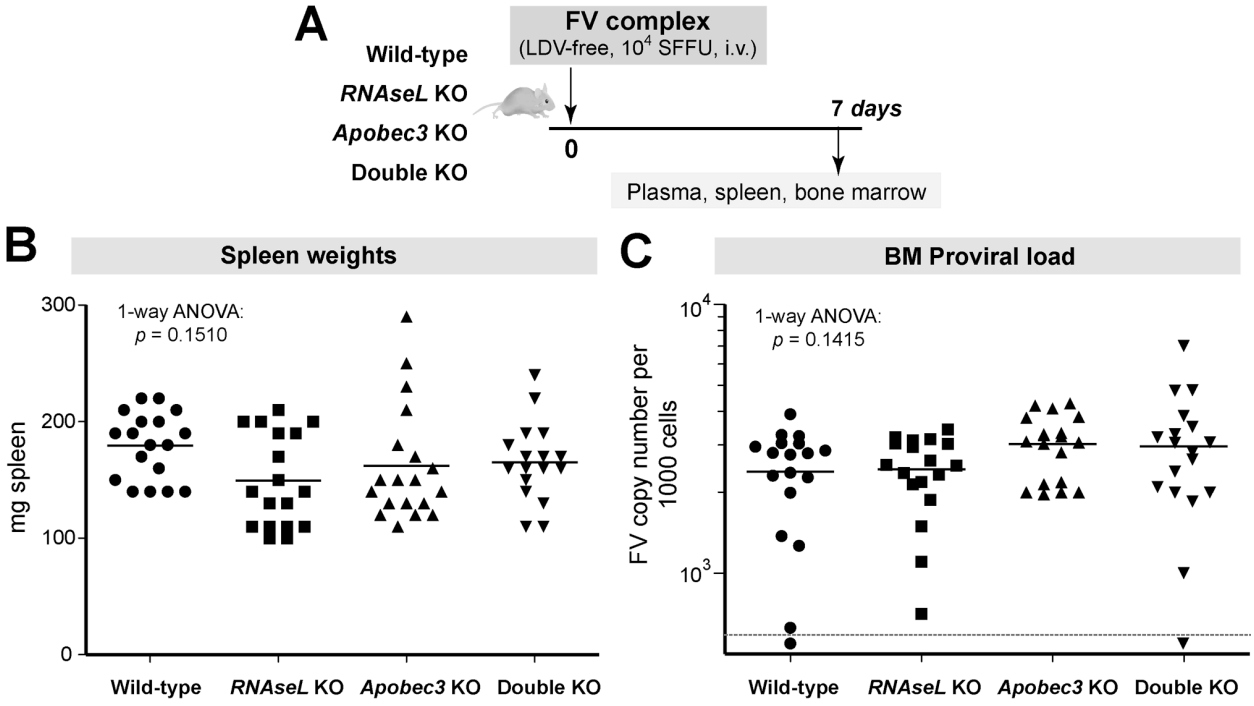
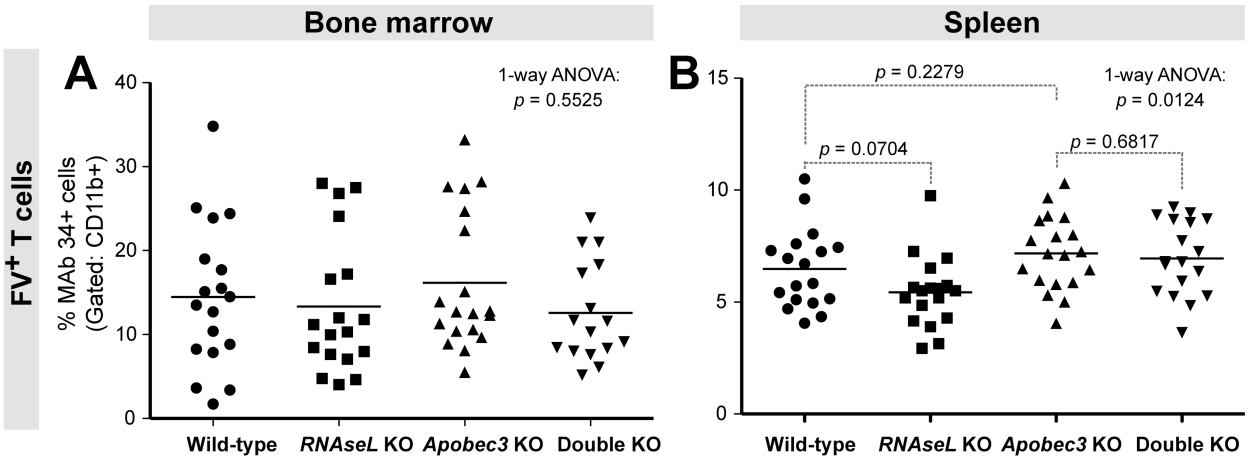
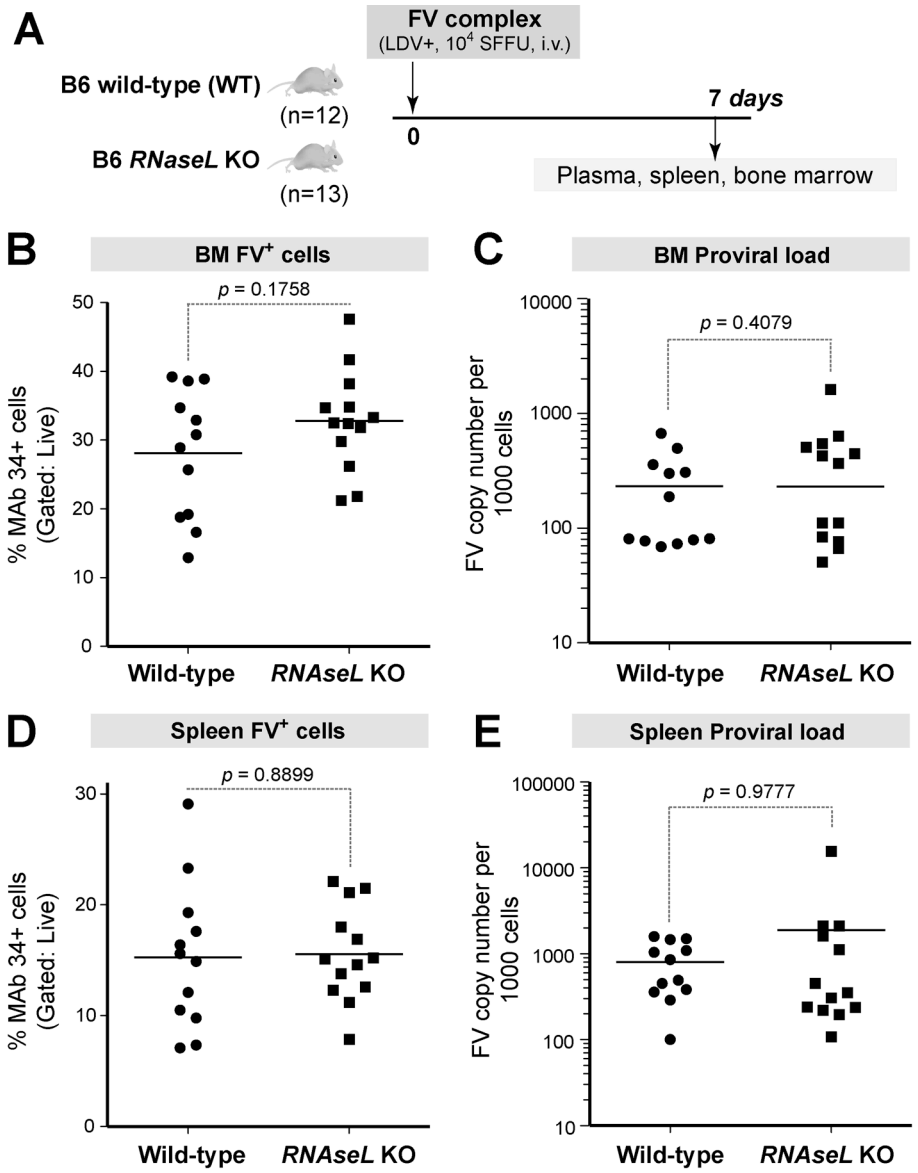


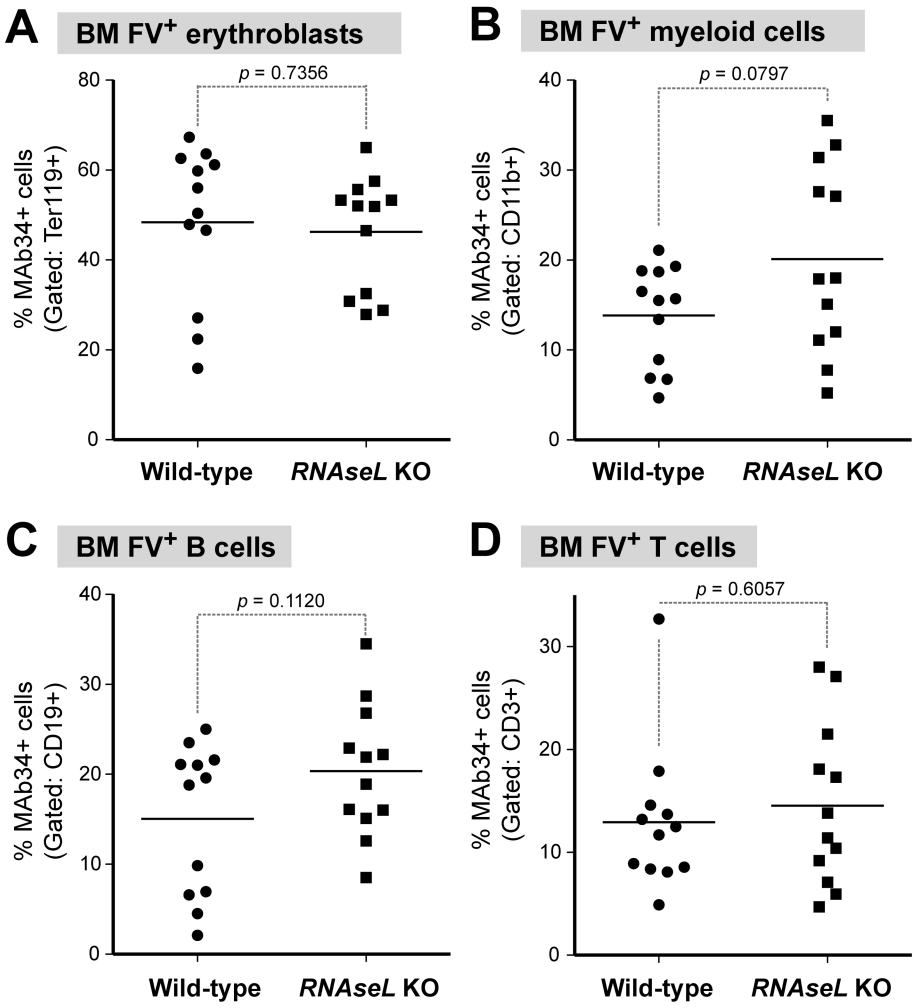
Supplementary Figure 1. *RNaseL* does not influence spleen weight or proviral load in acute FV infection. (A) Infection timeline. Samples were harvested at 7 dpi for analyses. Data were pooled from 3 independent experiments. (B) Spleen mass. (C) BM proviral load. BM DNA was evaluated for proviral FV copy number by qPCR and normalizing for cell equivalents. Log_{10} values are shown, and dashed lines correspond to the limit of detection of the assay. The data in panels B and C did not reach statistical significance following 1-way ANOVA. For both panels, each dot corresponds to an infected mouse, and bars correspond to mean values.



Supplementary Figure 2. *RNaseL* does not significantly inhibit acute FV infection in CD3+ T cells. WT, *RNaseL* KO, *Apobec3* KO, and double KO mice were infected with 10^4 SFFU of FV, and at 7 dpi, flow cytometry was used to distinguish CD3+ T cells from (A) BM and (B) splenocytes. Data were pooled from 3 independent infection cohorts. FV expression was detected using MAb 34. For both panels, each dot corresponds to an infected mouse, and bars correspond to mean values. Differences between the cohorts were evaluated by 1-way ANOVA. If the ANOVA was significant ($p<0.05$), differences between pairs of experimental groups were evaluated using 2-tailed Student's *t* test, with $p<0.05$ considered statistically significant



Supplementary Figure 3. Acute FV/LDV infection in WT versus *RNaseL* KO mice. (A) Infection timeline with the classical FV/LDV stock. At 7 dpi, BM and spleen samples were harvested for analyses. Data were pooled from 2 independent infection cohorts. (B) FV+ BM cells. MAb 34, a monoclonal antibody against the FV Glyco-Gag protein, was used to stain for flow cytometry. (C) BM proviral load. DNA was extracted from BM and qPCR was used to determine the amount of FV proviral DNA. Data were normalized to *Apobec3* DNA copies, with 2 copies = 1 cell equivalent. Log_{10} values are shown. (D) FV+ splenocytes based on MAb 34 flow cytometry. (E) Spleen proviral load. Similar to (C), qPCR was used, normalizing to *Apobec3* copies and expressing the data as log_{10} values. For all panels, each dot corresponds to an infected mouse, and bars correspond to mean values. *P* values were calculated using 2-tailed Student's *t* test, with $p<0.05$ considered statistically significant.



Supplementary Figure 4. *RNaseL* does not significantly inhibit acute FV infection in target cell subpopulations in the context of LDV co-infection. WT, *RNaseL* KO, *Apobec3* KO, and double KO mice were infected with 10^4 SFFU of FV, and at 7 dpi, BM and splenocytes were subjected to flow cytometric analyses. Data were pooled from 2 independent infection cohorts. BM cells were stained with antibodies to detect (A) erythroblasts, Ter119; (B) myeloid cells, CD11b; (C) B cells, CD19; and (D) T cells, CD3. FV expression was detected using MAb 34. For all panels, each dot corresponds to an infected mouse, and bars correspond to mean values. Differences between pairs of experimental groups were evaluated using 2-tailed Student's *t* test, with $p<0.05$ considered statistically significant.