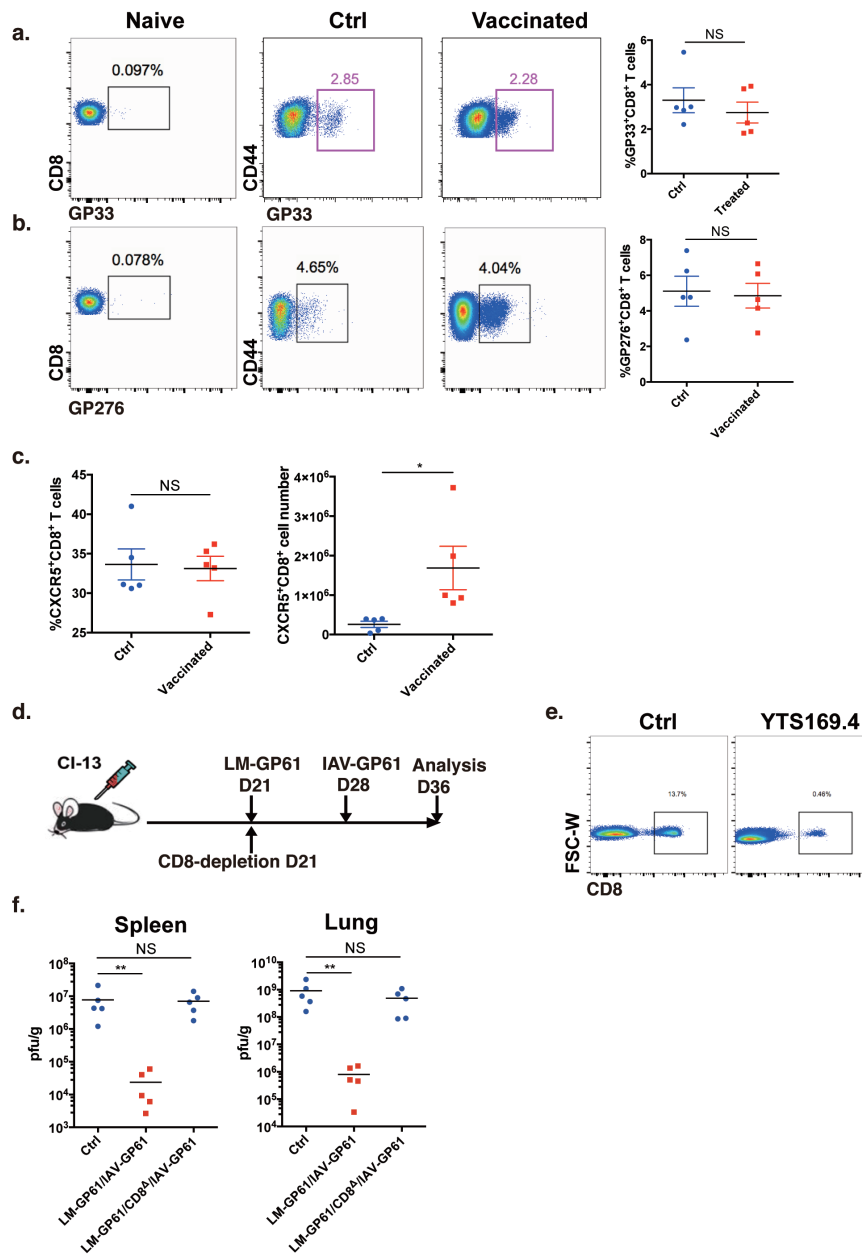
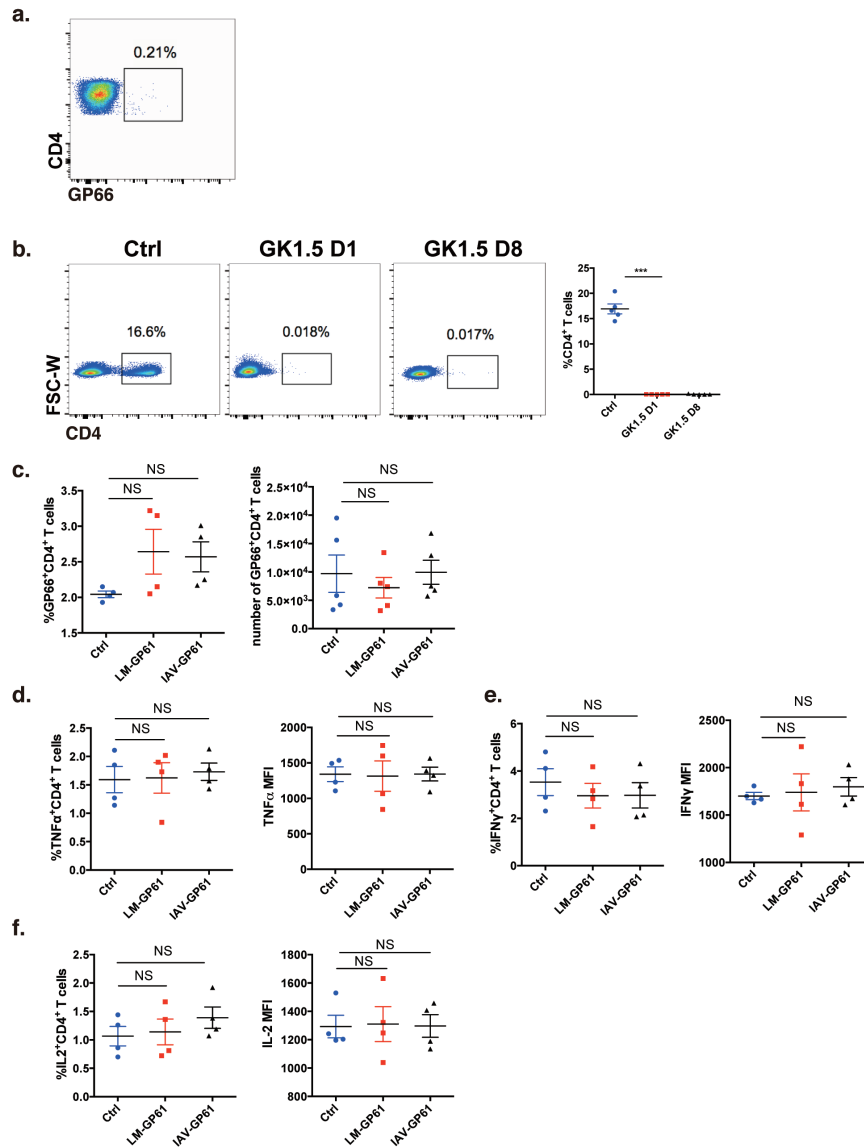


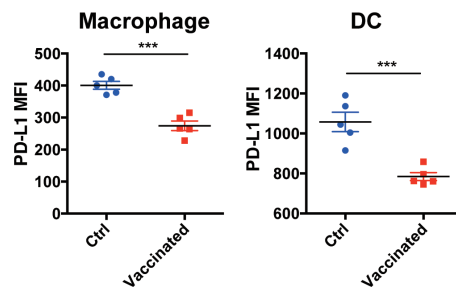
Supplementary Figure 1. The survival and immunopathology of control and vaccinated mice. (a) The survival present of control and vaccinated mice. **(b)** The sera levels of ALT and AST in control and vaccinated mice. **(c)** The bodyweight reduction of control and vaccinated mice. These data are representative of three independent experiments (n=4) and were analyzed by two-tailed unpaired *t*-tests **(a-b)**. Error bars denote s.e.m. NS, not significant.



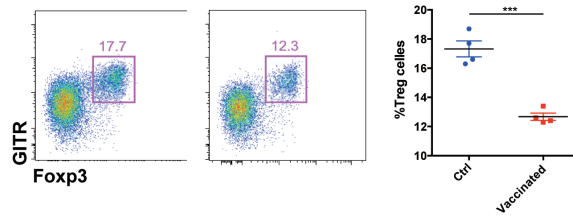
Supplementary Figure 2. Virus-specific CD8⁺ T cells are essential for the control of viral replication in the heterologous prime-boost vaccination. (a-b) Tetramer staining and frequency of GP33 and GP276-specific CD8⁺ T cells (n=5). (c) The frequency and number of CXCR5⁺CD8⁺ T cells in the spleens of control and vaccinated mice (n=5). (d) CD8⁺ T cell were depleted in the vaccinated mice at the time of priming. (e) Depletion efficiency of CD8⁺ T cell. (f) Viral titers in the indicated tissues (n=5). The data are representative of three independent experiments and were analyzed by two-tailed unpaired *t*-tests (a-c) and Mann-Whitney tests (e). Error bars denote s.e.m. **P*<0.05. NS, not significant.



Supplementary Figure 3. Single immunization with either LM-GP61 or IAV-GP61 could not significantly enhance CD4⁺ T cell response in chronic viral infection. (a) Tetramer staining of LCMV-GP66 on naïve CD4⁺ T cells. **(b)** The depletion efficiency of CD4⁺ T cell (n=5). **(c)** The frequency and number of LCMV specific GP66⁺CD4⁺ T cells in the spleens of control and vaccinated mice (n=5). **(d-f)** The cytokine production of LCMV-specific CD4⁺ T cells in the spleens of control and immunized mice (n=5) upon stimulation with an LCMV-specific peptide (GP61-77). MFI, mean fluorescence intensity. The data are representative of three independent experiments and were analyzed by two-tailed unpaired *t*-tests **(b-f)**. Error bars denote s.e.m. ****P*<0.001. NS, not significant.



Supplementary Figure 4. The expression levels of PD-L1 in macrophages and dendritic cells (DCs) from the spleens of control and vaccinated mice. The data are representative of three independent experiments (n=5) and were analyzed by two-tailed unpaired *t*-tests. Error bars denote s.e.m. *** $P < 0.001$.



Supplementary Figure 5. The frequency of regulatory T cells (Treg cells) in the spleens of control and vaccinated mice. The data are representative of three independent experiments (n=4) and were analyzed by two-tailed unpaired *t*-tests. Error bars denote s.e.m. *** $P < 0.001$.