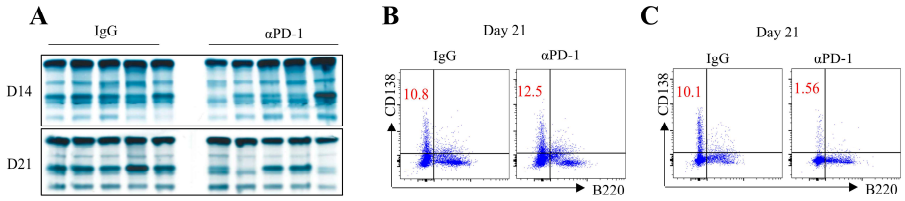
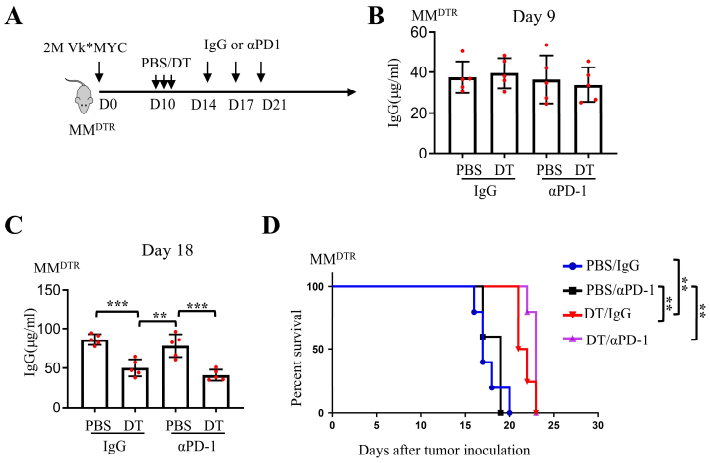
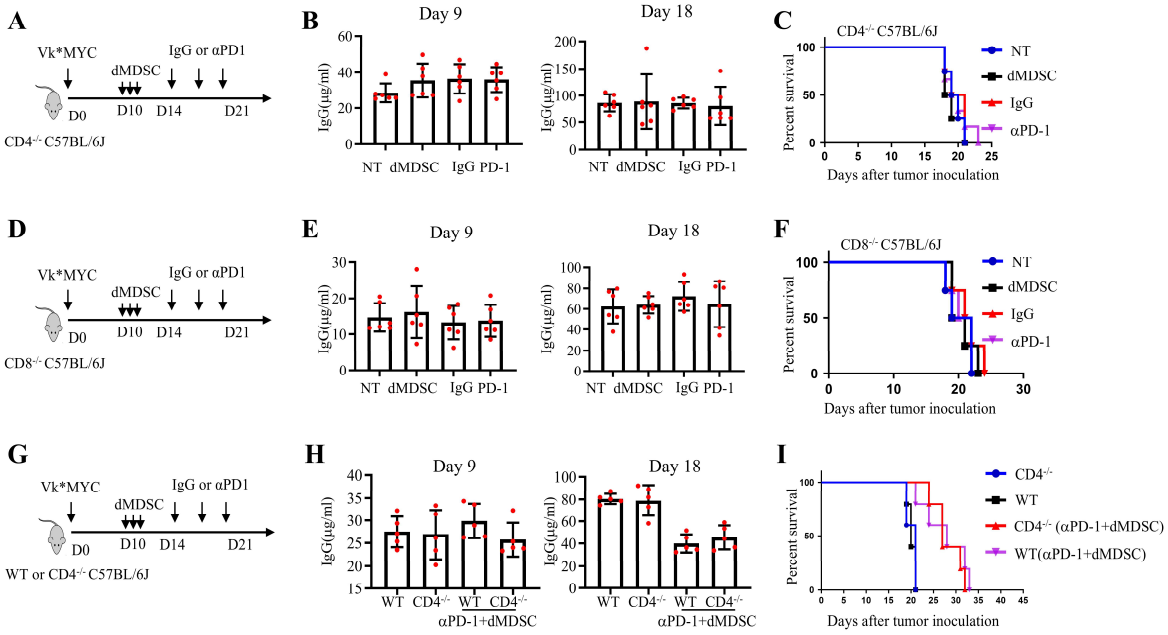


Supplementary Figure 1. Vk*MYC and 5TGM1 MM models exhibit different responses to PD-1 ICB

(**A-B**) C57BL/6 mice were inoculated with 0.5 × 10^6 Vk*MYC cells intravenously. After 14 days, mice randomly received intraperitoneal injections of 100 μg control IgG or αPD-1 every 3 days, for a total of three injections. Tumor burden was detected by measuring the level of IgG M-protein secreted by MM cells using serum protein electrophoresis (**A**), or representative histograms showing the percentages of $CD138^+$ $B220^-$ plasma cells in the BM (**B**). (**C**) C57BL/KaLwRij mice were inoculated intravenously with 2 × 10^6 5TGM1-luc cells and, on day 14, randomly received intraperitoneal injections of 100 μg control IgG or αPD-1 every 3 days for a total of three injections. Representative histograms showing the percentages of $CD138^+$ $B220^-$ plasma cells in the BM.



Supplementary Figure 2. Depleting macrophages inhibits tumor growth without affecting the response to PD-1 inhibitors in Vk*MYC MM. (**A**) MM^{DTR} mice were inoculated intravenously with 2×10^6 Vk*MYC cells and randomly received intraperitoneal injections of PBS or DT on day 10, followed by the treatment with IgG or αPD-1 (n = 5). Serum IgG levels were measured by ELISA on day 9 (**B**) and day 18 (**C**) after tumor inoculation. (**D**) Kaplan–Meyer survival plots of treated mice. Data are presented as mean ± SD. **P < 0.01; ***P < 0.001.



Supplementary Figure 3. CD4$^+$ T cells are dispensable for the restored PD-1 inhibitor response induced by MDSC depletion in Vk*MYC MM.

(**A-C**) WT, CD4$^{-/-}$ C57BL/6J mice were inoculated intravenously with 0.5 × 10^6 Vk*MYC cells and randomly received intraperitoneal injections of irrelevant peptides, peptibodies, IgG or αPD-1 on day 10. Serum IgG/M-protein levels were measured by ELISA on day 9 and day 18 after tumor inoculation (**B**, n = 6), and Kaplan–Meyer survival plots of treated mice (**C**, n = 6). (**D-F**) Wild-type, CD8$^{-/-}$ C57BL/6J mice were inoculated intravenously with 0.5 × 10^6 Vk*MYC cells and randomly received intraperitoneal injections of irrelevant peptides, peptibodies, IgG or αPD-1 on day 10. Serum IgG/M-protein levels were measured by ELISA on day 9 and day 18 after tumor inoculation (**E**, n = 6), and Kaplan–Meyer survival plots of treated mice (**F**, n = 6). (**G-I**) Wild-type or CD4$^{-/-}$ C57BL/6J mice were inoculated intravenously with 0.5 × 10^6 Vk*MYC cells and randomly received intraperitoneal injections of irrelevant peptides or peptibodies on day 10, followed by the treatment with IgG or αPD-1. Serum IgG/M-protein levels were measured by ELISA on day 9 and day 18 after tumor inoculation (**H**, n = 5), and Kaplan–Meyer survival plots of treated mice (**I**, n = 5).