**Supplementary Figure Legends**

**Supplementary Figure S1**. **Anti-PD-1 reduces tumor weight and modulates PD-1 expressing intratumor T cells in anti-PD-1-sensitive tumor**. Groups of B6 WT mice (n=5-8) were s.c. injected with (A and B) MC38 tumor (1 x 106 cells) or (C and D) AT3 tumor (1 x 106 cells) on day 0, and treated with 250 μg of control Ig or anti-PD-1 on (A and B) day 10 or (C and D) day 14. Tumors were harvested two or three days after antibody treatments for flow cytometric analyses. (A and C) Tumor weights, (B and D) (*upper panel*) frequencies, and (*lower panel*) cell numbers (per gram of tissue) of CD45.2+ cells, CD4+ T cells, CD8+ T cells, PD-1-expressing CD4+ T cells, PD-1-expressing CD8+ T cells between control Ig- and anti-PD-1-treated mice are shown. Statistical differences in (A and C) tumor weight, (B and D) frequencies, and cell numbers of indicated cell subsets between control Ig- and anti-PD-1-treated mice were determined by an unpaired T test (\* < p 0.05; \*\* p < 0.01; \*\*\* < 0.001; p \*\*\*\* < 0.0001). Data shown are pooled from (A and B) twelve and (C and D) seven independent experiments, and presented as mean ± SD with individual symbols representing individual mice. Data shown for frequencies of (B and D) PD-1-expressing CD4+ T cells, PD-1-expressing CD8+ T cells between control Ig- and anti-PD-1-treated mice are the same data set as shown in Figure 1E and 1F.

**Supplementary Figure S2**. **Anti-PD-1 therapy mAb does not compete for the binding of PD-1 with the anti-PD-1 flow cytometry staining mAb**. Groups of B6 WT mice (n=4) were s.c. injected with MC38 tumor (1 x 106 cells) and tumors were harvested to prepare tumor cell suspensions. Tumor suspensions were incubated with unconjugated control Ig or unconjugated anti-PD-1 (clone RMP1-14; therapy) (5 μg/ml) for 20 minutes on ice, and then washed twice. Antibody-blocked tumor suspensions were then used for flow cytometric analyses. Histograms shown are PD-1-FITC (clone J43; staining) staining on intratumor CD8+ T cells (gated on CD8+ and TCRβ+ cells) in control Ig-blocked (shaded histogram) and anti-PD-1 (open histogram) tumor suspensions, representative of four individual mice.

**Supplementary Figure S3. Anti-PD-1 mAb reduces PD-1 expression on PD-1-expressing T cells**. Groups of B6 WT mice (n=5-8) were s.c. injected with (A and B) MC38 tumor (1 x 106 cells) or (C and D) AT3 tumor (1 x 106 cells) on day 0. Tumor-bearing mice were treated with 250 μg of control Ig or anti-PD-1 on (A and B) day 10 or (C and D) day 14, and tumors were harvested two or three days after antibody treatments for flow cytometric analyses. PD-1 MFI of the indicated CD4+ and CD8+ T cells and representative histogram plots (Dashed histogram: isotype; shaded histogram: control Ig-treated; open histogram: anti-PD-1-treated) between control Ig- and anti-PD-1-treated mice are shown. Statistical differences in PD-1 MFI of indicated cell subsets between control Ig- and anti-PD-1-treated mice were determined by an unpaired T test (\*\*\*\* p < 0.0001). Data shown are pooled from (A and B) twelve and (C and D) seven independent experiments, and presented as the mean ± SD with individual symbols representing individual mice.

**Supplementary Figure S4.** **Frequency of PD-1+ CD8+ T cells maintained in anti-PD1-resistant Renca tumors**. Groups of Balb/c WT mice (n=5-8) were s.c. injected with Renca tumor cells (2 x 105) on day 0. (A) Tumor-bearing mice were treated with 250 μg of control Ig or anti-PD1 on days 8, 12, and 16. Tumor growth was measured using a digital caliper, and tumor sizes are presented as mean ± SEM. (B, C, and D) Tumor-bearing mice were treated with 250 μg of control Ig or anti-PD1 on day 8, and tumors were harvested two days after mAb treatments for tumor weight and flow cytometric analyses. (B) Tumor weights and (C) frequencies of PD1-expressing CD4+ T cells and PD1-expressing CD8+ T cells between control Ig- and anti-PD1-treated mice are shown. Statistical differences in (C) frequencies of respective cell subsets between control Ig- and anti-PD1-treated mice were determined by an unpaired T test (\*\* p < 0.01). (D) PD1 MFI of the indicated CD4+ and CD8+ T cells and representative histogram plots (Dashed histogram: isotype; shaded histogram: control Ig-treated; open histogram: anti-PD1-treated) between control Ig and anti-PD1-treated mice are shown. Statistical differences in PD1 MFI of indicated cell subsets between control Ig- and anti-PD1-treated mice were determined by an unpaired T test (\* < p 0.05; \*\*\* < 0.001). (B, C, and D) Data shown are presented as the mean ± SD with individual symbols representing individual mice.

**Supplementary Figure S5. Anti-Tim3 and anti-PD1 sensitivity correlates with reduced frequency of PD1 expressing CD8+ T cells**. Groups of (A and B) Balb/c and (C and D) B6 WT mice (n=5-10) were s.c. injected with (A) CT26 tumor (2 x 105 cells), (B) CT26 tumor (1 x 105 cells) or (C and D) AT3 tumor (1 x 106 cells) on day 0. (A and C) Tumor-bearing mice were treated with 250 μg of control Ig, anti-Tim3 and/or anti-PD1 on (A) day 10 or (C) day 14, and tumors were harvested three days after antibody treatments for flow cytometric analyses. Frequencies of PD1-expressing CD4+ and CD8+ T cells are shown. Data are presented as the mean ± SD with individual symbols representing individual mice. Statistical differences in the frequencies of PD1-expressing CD4+ T cells and CD8+ T cells between control Ig- , anti-Tim3, anti-PD1, and anti-Tim3 + anti-PD1-treated mice were determined by an unpaired T test (\* p < 0.05; \*\* p< 0.01). (A) Data shown are pooled from two independent experiments. (B) Tumor-bearing mice were treated with 250 μg of control Ig, anti-Tim3 and/or anti-PD1 on days 10, 14, and 18. Tumor growth was measured using a digital caliper, and tumor sizes are presented as mean ± SEM. Statistical differences in tumor sizes between control Ig-, anti-Tim3-, anti-PD1-, and anti-Tim3 + anti-PD1-treated mice were determined by an unpaired T test (Day 16: control Ig vs anti-Tim3 + anti-PD1 p= 0.0077) (Day 18: control Ig vs anti-Tim3 + anti-PD1 p= 0.0015) (Day 20: control Ig vs anti-Tim3 + anti-PD1 p= 0.0005) (Day 22: control Ig vs anti-Tim3 + anti-PD1 p= 0.0003). (D) Tumor-bearing mice were treated with 250 μg of control Ig, anti-Tim3 and/or anti-PD1 on days 14, 18, 22, and 26. Tumor growth was measured using a digital caliper, and tumor sizes are presented as mean ± SEM. Statistical differences in tumor sizes between control Ig-, anti-Tim3-, anti-PD1-, and anti-Tim3 + anti-PD1-treated mice were determined by an unpaired T test. Data are representative of two independent experiments. Tumor growth data for control Ig- and anti-PD1-treated mice shown in (D) are the same data set as shown in Figure 5D.

**Supplementary Figure S6. Anti-PD-1/PD-L1 anti-tumor effect is FcR-independent**. Groups of B6 WT and gene-targeted mice (n=5-8) as indicated were s.c. injected with MC38 tumor (1 x 106 cells) on day 0, and treated with 250 μg of control Ig or (A) anti-PD-1 or (B) anti-PD-L1 on days 6, 10, and 14. Tumor growth was measured using a digital caliper, and tumor sizes are presented as mean ± SEM. Statistical differences in tumor sizes between cIg- and anti-PD-1/PD-L1-treated mice were determined by an unpaired T test (\*\* p < 0.01; \*\*\* < 0.001; p \*\*\*\* < 0.0001). Data are representative of (A) two and (B) one independent experiments.

**Supplementary Figure S7. PD-1-expressing T cells are predominantly found in the tumor microenvironment**. Groups of B6 WT mice (n=4-5) were s.c. injected with (A) MC38 tumor (1 x 106 cells) or (B) AT3 tumor (1 x 106 cells) on day 0, and treated with 250 μg of control Ig on (A) day 10 or (B) day 14. Organs indicated from tumor-bearing mice were harvested three days after antibody treatment for flow cytometric analyses. Frequencies of PD-1 of (*left panel*) CD4+ and (*right panel*) CD8+ T cells from tumor-bearing mice are shown. Data are shown as mean ± SD with individual symbols representing individual mice. DLN: Draining lymph node; NDLN: Non-draining lymph node.

**Supplementary Figure S8. PD1 MFI on CD8+ T cells predicts tumor aggressiveness and response to anti-PD1 mAb in MC38 tumor**. Analysis of covariance (ANCOVA) was applied to test the association between the PD1 MFI on CD8+ PD1lo (MC38) or PD1hi (AT3) T cells and the tumor weight and the interaction between the two slopes. Plots of PD1 MFI on CD8+ PD1+/- T cells against the weight of tumors (monitored 2 to 3 days after the first injection of mAb) from mice inoculated with MC38 (*left panels*) and AT3 (*right panels*) tumor cells and treated with control Ig (solid circles) or anti-PD1 Ab (open circles). Dashed lines correspond to the slopes and associated standard error as estimated by the ANCOVA model for each treatment group. Data sets used are the same as data sets shown in Figure 6. (\* p < 0.05; \*\* p < 0.01; \*\*\*\* p < 0.0001). Wei = weight ; Trt = treatment ; Int = interaction.