**Supplementary Figure S1. *In vitro* PD-L1 expression in MC38, CT26-NY-ESO-1, B16-F10, Renca, CMS5a and A20 treated with or without IFN-α, IFN-β, IFN-γ, TNF-α, IL-2, IL-4, TGF-β1 or GM-CSF.**

Cells were treated with IFN-α (1,000 IU/mL), IFN-β (1,000 IU/mL), IFN-γ (1,000 IU/mL), TNF-α (20 ng/mL), IL-4 (20 ng/mL), TGF-β1 (5 ng/mL) or GM-CSF (20 ng/mL) for 24 hours and were subsequently subjected to flow cytometry. Gray, isotype control; blue, untreated; red, stimulant-treated. Representative data are shown from two to three independent experiments.

**Supplementary Figure S2. *In vitro* PD-L2 expression in MC38, CT26-NY-ESO-1, B16-F10, Renca, CMS5a and A20 treated with or without IFN-α, IFN-β, IFN-γ, TNF-α, IL-2, IL-4, TGF-β1 or GM-CSF.**

Cells were treated with IFN-α (1,000 IU/mL), IFN-β (1,000 IU/mL), IFN-γ (1,000 IU/mL), TNF-α (20 ng/mL), IL-4 (20 ng/mL), TGF-β1 (5 ng/mL) or GM-CSF (20 ng/mL) for 24 hours and were subsequently subjected to flow cytometry. Gray, isotype control; blue, untreated; red, stimulant-treated. Representative data are shown from two to three independent experiments.

**Supplementary Figure S3. *In vivo* PD-L2 expression in APCs from MC-38 tumor.**

TILs were prepared on day 14, and the expression of PD-L1 and PD-L2 in APCs (CD45+MHCII+CD11c+CD11b+ cells) was examined. MC-38-L2 was used as a positive control. Gray, isotype control; blue, APCs; red, MC-38-L2 cell line. Representative data are shown from two to three independent experiments.

**Supplementary Figure S4. Effector CD8+ T cells detected by CD44+CD62L-CD8+ T cells, PD-1+CD8+ T cells, and cytokine-producing CD8+ T cells in TILs from MC-38 tumors.**

TILs were prepared from MC-38 tumors on day 14 and CD44+CD62L-CD8+ TILs, PD-1+CD8+ TILs, and TNF-α+IFN-γ+CD8+ TILs were examined. Representative data are shown from two to three independent experiments.

**Supplementary Figure S5.** ***In vivo* tumor growth in nude, CD4+ T cell or CD8+ T cell-depleted mice.**

**(A)** Tumor cells (1.0×106) were injected subcutaneously on day 0 in nude mice and tumor growth was monitored twice a week (n = 5 per group). **(B, C)** Tumor cells (1.0×106) were injected subcutaneously on day 0 in immunocompetent wild-type mice, and anti-CD4 mAb **(B)** or anti-CD8β mAb **(C)** were injected intraperitoneally on days -1, 0, and every seven days after tumor injection. Tumor growth was monitored twice a week (n = 8 per group). N.S., not significant; \*, *P* < 0.05. *In vivo* experiments were performed at least twice.

**Supplementary Figure S6.** **Effector CD8+ T cells detected by CD44+CD62L-CD8+ T cells, PD-1+CD8+ T cells, and cytokine-producing CD8+ T cells in TILs from MC-38, MC-38-GFP, or MC-38-L2 tumors.**

TILs were prepared from MC38-, MC-38-GFP-, or MC-38-L2 tumors on day 14 and CD44+CD62L-CD8+ TILs, PD-1+CD8+ TILs, and TNF-α+IFN-γ+CD8+ TILs were examined. Representative data are shown from two to three independent experiments.

**Supplementary Figure S7.** ***In vivo* tumor growth treated with anti-PD-1 and/or anti-PD-L2 mAb in immunocompetent mice.**

MC-38-L2 cells (1.0×106) were injected subcutaneously on day 0 in immunocompetent mice, and ICB as indicated was administered on days 3, 6, and 9. Tumor growth was monitored twice a week (n = 8 per group). N.S., not significant; \*\*, *P* < 0.01; \*\*\*, *P* < 0.001. *In vivo* experiments were performed at least twice.

**Supplementary Figure S8.** ***In vivo* tumor growth treated with PD-1 signal blockades in nude, CD4+ T cell or CD8+ T cell-depleted mice.**

**(A)** Antitumor efficacies of various ICBs including combinations against MC-38-L2 and CT26-NY-ESO-1-L2 tumors in nude, CD4+ T cell or CD8+ T cell-depleted mice. Left: MC-38-L2 cells (1.0 × 106) were injected subcutaneously on day 0, and ICB as indicated were administered on days 3, 6, and 9. Tumor growth was monitored twice a week (n = 8 per group).Right: CT26-NY-ESO-1-L2 cells (1.0 × 106) were injected subcutaneously on day 0, and ICB as indicated were administered on days 7, 10, and 13. Tumor growth was monitored twice a week (n = 8 per group). **(B)** *In vivo* efficacies of anti-PD-L2 mAb against parental tumors or GFP-expressing tumors in nude mice. Left: MC-38 or MC-38-GFP cells (1.0 × 106) were injected subcutaneously on day 0, and ICB as indicated were administered on days 3, 6, and 9. Tumor growth was monitored twice a week (n = 8 per group).Right: CT26-NY-ESO-1 or CT-26-NY-ESO-1-GFP cells (1.0 × 106) were injected subcutaneously on day 0, and ICB as indicated were administered on days 7, 10, and 13. Tumor growth was monitored twice a week (n = 8 per group). N.S., not significant; \*, *P* < 0.05; \*\*, *P* < 0.01; \*\*\*, *P* < 0.001. *In vivo* experiments were performed at least twice.

**Supplementary Figure S9.** **Effector CD8+ T cells detected by CD44+CD62L-CD8+ T cells, PD-1+CD8+ T cells, and cytokine-producing CD8+ T cells in TILs from MC-38-L2 tumors.**

TILs were prepared from MC-38-L2 tumors on day 14 and CD44+CD62L-CD8+ TILs, PD-1+CD8+ TILs, and TNF-α+IFN-γ+CD8+ TILs were examined (n = 8 per group). Top: Representative data are shown from two to three independent experiments. Bottom: Summary of the frequency of each fraction. \*, *P* < 0.05; \*\*, *P* < 0.01; \*\*\*, *P* < 0.001. *In vivo* experiments were performed at least twice.

**Supplementary Figure S10. *In vitro* PD-L1 and PD-L2 expressions by MC-38-L1KO and MC-38-L1KO-L2 treated with or without IFN-γ and *in vivo* tumor growth of those tumors.**

Left: *In vitro* PD-L1 and PD-L2 expressions by MC-38-L1KO and MC-38-L1KO-L2 treated with or without IFN-γ. Gray, isotype control; blue, untreated; red, IFN-γ-treated. Representative data are shown from two to three independent experiments. Right: *In vivo* tumor growth of MC-38-, MC-38-L1KO-, MC-38-L1KO-GFP-, MC-38-L1KO-L2 tumors in nude mice. Cells (1.0×106) were injected subcutaneously on day 0 in nude mice. Tumor growth was monitored twice a week (n = 5 per group).N.S., not significant. *In vivo* experiments were performed at least twice.

**Supplementary Figure S11. The scattergram and real number of pearson correlations between expression levels (RPKM) of immune-related genes and *CD274* or *PDCD1LG2* in BLCA, GC, HNSC, LUAD and LUSC.**

In LUSC, *PDCD1LG2* expression had relatively good correlations with immune-related gene expressions compared with *CD274* expression.

**Supplementary Figure S12. The relationship between *CD274* or *PDCD1LG2* expressions and survival in RCC and LUSC.**

Patients from TCGA datasets were divided into two groups (high and low) using the median expression level of *CD274* or *PDCD1LG2*, and OS was compared between the two groups. Top: In RCC, no correlation between *CD274* (left) or *PDCD1LG2* (right) expression and survival was observed. Bottom: In LUSC, high expression of *CD274* (left) or *PDCD1LG2* (right) equally correlated with long survival.