

Supplemental figure legends

Supplemental figure 1. Radiation induced upregulation of CD73 and PD-L1 on pancreatic cancer cells.

Expression of CD73 (**A**, KCKO and **B**, KP2) and PD-L1(**C**, KCKO and **D**, KP2) on surface of KCKO and KP2 cells 1, 2 and 3 days after irradiation with single dose of 15 Gy was analyzed by flow cytometry. In each subfigure (A, B, C or D), left panel shows histogram of one representative flow cytometry data set and right panel shows mean fluorescence intensity (MFI) from three replicates, presented as mean \pm SEM. Data was analyzed by one-way ANOVA with Dunnett posttest. *, $P < 0.05$, **, $P < 0.01$, ***, $P < 0.001$, compared with untreated (day 0).

Supplemental figure 2. SBRT increases expression of CD73 and PD-L1 in orthotopic PDAC model.

Mice bearing KCKO-Luc orthotopic pancreatic tumors were treated with SBRT as in Figure 1. On day 11 (1 day after SBRT), CD73(**A**) and PD-L1(**2**) expression was analyzed by flow cytometry gating on tumor cells. **A**. CD73 expression on tumor cells. Left, representative flow cytometry plots. Right, MFI of CD73 on tumor cells, expressed as mean \pm SEM from 5 mice/group and analyze by Student *t* test. *, $P < 0.05$. **B**. PD-L1 expression on tumor cells. Left, representative flow cytometry plots. Right, MFI of PD-L1 on tumor cells, expressed as mean \pm SEM from 5 mice/group and analyzed by Student *t* test. *, $P < 0.05$.

Supplemental figure 3. Triple therapy with SBRT, anti-CD73 and anti-PD-L1 enhances activation of CD8 and CD4 cells in spleen from the orthotopic model of murine pancreatic cancer.

Mice bearing KCKO-Luc orthotopic pancreatic cancer were treated as in Figure 1 and sacrificed on day 14. Immune cells in spleen were determined by flow cytometry. Results are expressed as mean \pm SEM from five mice / group and analyzed by ANOVA with Dunnett posttest. Significance is indicated by *, $p < 0.05$.

Supplemental figure 4. Gating strategy for flow cytometry analysis.

Mice bearing KCKO-Luc orthotopic pancreatic cancer were treated as in Figure 1 and sacrificed on day 14. Tumor-infiltrating immune cells were determined by flow cytometry. **A**. T cells gating strategy. **B**. Myeloid cells gating strategy. **C**. DCs gating strategy.

Supplemental figure 5. The Luminex analysis of cytokines and chemokines in pancreatic cancer.

Mice bearing KCKO-Luc orthotopic pancreatic tumors were treated as in Figure 1. Mice were sacrificed on day 14 post tumor cell injection; tumor cytokines and chemokines were determined by multiplex Luminex assay. Results are expressed as mean \pm SEM from five mice per group and analyzed by one-way ANOVA with Dunnett post-test. Significances are indicated by *, $p < 0.05$, and **, $p < 0.01$, ***, $p < 0.001$, compared with untreated group.

Supplemental figure 6. Chemotherapy (Gemcitabine/nab-paclitaxel) following combination treatment of anti-CD73 and anti-PD-L1 delayed tumor growth in orthotopic PDAC mouse model.

KCKO-Luc orthotopic pancreatic cancer model was established as in Figure 1 and treated with gemcitabine (100mg/kg, i.p.) and nab-paclitaxel (100mg/kg, i.v.) on day 5 and 9 post tumor implantation. 10 mg/kg of anti-CD73, anti-PD-L1 or isotype control IgG were administered twice a week starting on day 13 post tumor implantation. **A.** Tumor growth curve was determined by IVIS imaging twice a week. Data shown are mean of IVIS value \pm SEM from 10 mice/group. **B.** Kaplan-Meier survival curve. *, $P < 0.05$, **, $P < 0.01$, compared with untreated group by one-way ANOVA with multiple comparison (adjusted by Bonferroni method) for growth or by log-rank (Mantel-Cox) test with multiple comparison (adjusted by Bonferroni method) for survival curve. IVIS, in vivo imaging system.