**SUPPLEMENTARY FIGURE LEGENDS**

**Figure S1. CD11b+CD11c+MHC-II+** **cells exhibit DC phenotype and accumulate at multiple metastatic sites**

(A) Myeloid cell subsets among CD45+ liver NPC from sham-operated naïve mice or 3.5 wk orthotopic LMP-bearing mice. (B) Frequencies of myeloid subsets among total live lung cells from naïve or s.c. LMP-bearing mice with means ± SEM shown. (C) Representative plots showing gating scheme for CD11b+ DC in liver NPC sample from tumor-bearing mouse. Total CD11chiMHC-IIhi cells among CD45+ NPC are gated and then subsetted on the basis of CD11b expression. CD11b+ DC (red) are overlaid on total CD45+ NPC (blue), including gated KC/TAM. (D, E) Representative plots showing marker expression by CD11chiMHC-IIhi DC subsets (E) and F4/80+CD11bint KC/TAM (E) from the liver of pancreatic tumor-bearing mice. Isotype control stains were used to set gates (D, E) and are shown in gray (E). (F) Liver tissue sections from naïve and 3.5 wk pancreatic tumor-bearing mice stained for CD11b. Scale bar, 100 μm. (G) Micrometastatic liver tissue section stained with the indicated antibodies. Scale bar, 100 μm. (H) Relative cytokine levels measured by protein array analysis of supernatants from CD11b+ subsets cultured ex vivo for 24 hr. \*, p<0.05; \*\*\*, p<0.001 by Student’s *t*-test comparing tumor-bearing to naïve mice.

**Figure S2. PDAC cells produce large amounts of GM-CSF and stimulate Mo-DC differentiation**

(A, B) Marker expression by CD45.1+CD11b+CD11c+MHC-II+ cells from the liver of tumor-bearing mice 5 d following CD45.1+ Mo transfer, with means ± SEM shown. (C) BM Mo from naïve mice cultured in the presence of CM from 3T3 or LMP cells or cocultured with LMP cells for 2 d prior to flow cytometric analysis. (D) Cytokine levels measured by multiplex analysis of 24 hr supernatants from 3T3 and LMP PDAC cells.

**Figure S3. Liver DC from tumor-bearing mice efficiently activate T cells in conventional assays**

(A-C) Liver DC from naïve or tumor-bearing were cocultured at the indicated ratios with syngeneic splenocytes in the presence of αCD3 (A) or with naïve OT-II CD4 T cells in the presence of OVA peptide (ISQ) (B, C). T cell proliferation as measured by 3H-thymidine incorporation (A, B) and cytokine production by multiplex analysis (C) after 3 d. Mean CPM ± SEM for multiple cocultures shown (n=2-4). \*, p<0.05; \*\*\*, p<0.001; \*\*\*\*, p<0.0001 by Student’s *t*-test (A) or one-way ANOVA with *post hoc* Tukey’s test (B).

**Figure S4. Metastasis-associated DC stimulate nTreg proliferation while suppressing CD8 T cells through PD-1 ligand expression**

(A) Micrometastatic liver tissue section stained with the indicated antibodies. Scale bar, 100 μm. p-H3, phosphorylated histone H3. (B, E-I) TLv-DC were cocultured with CFSE-labeled CD4 T cells from naïve (B, E-G) or pan T cells from tumor-bearing (H, I) mice in the presence of the indicated antibodies for 3-4 d prior to flow cytometric analysis. Mean frequencies ± SEM of specified cells in separate cocultures (n=3-5) are shown and all experiments were performed at least twice with similar results. (C) Helios expression by CD4+Foxp3+ cells from naïve and micrometastatic liver with means ± SEM shown. (D) CFSE-labeled liver NPC from naïve and tumor-bearing mice were cultured ex vivo for 3 d prior to flow cytometric analysis of CD4 T cells. (J) Pancreatic tumor weights with medians shown for *Foxp3DTR* tumor hosts treated with PBS or DT. (K) Metastatic burden with medians shown for *Foxp3DTR* mice treated with PBS or DT in the experimental metastasis model. \*, p<0.05; \*\*, p<0.01; \*\*\*, p<0.001; \*\*\*\*, p<0.0001 by Student’s *t*-test (C, E, G-I), one-way ANOVA with *post hoc* Tukey’s test (F), or Mann-Whitney *U*-test (K).

**Figure S5. MGL2+ cells exhibit DC phenotype and their depletion activates multiple lymphocyte populations**

(A) Marker expression by total MGL2+CD45+ liver NPC from pancreatic tumor-bearing mice. (B) Micrometastatic liver from pancreatic tumor-bearing mouse stained with the indicated antibodies. Scale bar, 100 μm. (C) MGL2 expression by CD45.1+CD11b+CD11c+MHC-II+ cells from the liver of tumor-bearing mice 5 d following CD45.1x129 F1 Mo transfer. (D) MGL2+CD11c+ cells among total CD11b+ BM Mo following indicated treatment. (E, F) CD11b+CD11c+MHC-II+ cells among CD45+ NPC (D) and MGL2 expression by CD11b+CD11c+MHC-II+ cells (E) in naïve mice or 14 d following i.s. tumor cell injection. (G) CD11c and MGL2 expression by CD45+ cells from primary tumors and livers of 4 wk tumor-bearing mice, and frequencies of MGL2+CD11b+CD11c+MHC-II+ cells. (H-J) Lymphocyte frequencies and marker expression in *Mgl2DTR* tumor hosts after 5 d of PBS or DT treatment. Means ± SEM are shown for all graphs. \*\*, p<0.01 by Student’s *t*-test.

**Figure S6. Blocking PD-L2 reduces metastasis without affecting primary tumor burden**

(A) Pancreatic tumor weights with medians shown for mice treated with αPD-L2 or control antibodies for 3 wk, starting 2 wk after tumor implantation. (B) Primary tumor weight and liver metastatic burden for individual mice are plotted. Spearman correlation coefficients and associated p-values for isotype control (left) and αPD-L2 (right) antibody-treated mice are shown.

**Figure S7. PD-L2+ and MGL+ cells are present in human PDAC tissues**

(A, B) Metastatic liver tissue sections from PDAC patient stained for PD-L2 (A) or MGL (B). Scale bar, 100 μm. (C, D) Matched gene expression values (RSEM) for indicated gene pairs, obtained from the TCGA PDAC dataset (n=179). Spearman correlation coefficients and associated p-values are shown.

**Figure S8. Development and function of CD11b+ DC in PDAC metastasis**

(A-C) Depiction of the CD11b+ DC-driven immune response associated with PDAC metastasis. (A) Developing metastases are bordered by dense networks of PD-1 ligand-expressing CD11b+ DC, which derive from infiltrating Mo in response to tumor-secreted GM-CSF. These DC orchestrate the metastasis-associated immune response in various ways, creating a microenvironment enriched with Treg and deficient in cytotoxic lymphocytes like CD8 T cells. (B) PD-L2 is exclusively expressed by CD11b+ DC in the metastatic microenvironment and blocking this molecule unleashes CD8 T cell-mediated tumor immunity, leading to a reduction in metastatic burden (reflected in pale coloration of tumor cells). (C) MGL2 is also selectively expressed by metastasis-associated CD11b+ DC, and depleting cells on the basis of this marker leads to a reduction in Treg, activation of multiple cytotoxic lymphocyte populations, and inhibition of metastasis development.