**Supplemental Figure S1.** Representative plots illustrating the gating strategy for analyzing infiltrating immune cells in the pancreas. Individual, viable leukocytes from dissociated pancreas were selected by forward and side scatter gating, the exclusion of dead cells using Fixable Viability Dye (eFluor™ 780), and selective gating of CD45 (APC). **Group 1:** stained with antibodies to CD11b (PE/Cy7), Gr1 (PerCP), CD11c (PE), and F4/80 (Alexa Fluor® 488), were selectively gated for CD11b+ cells (left panel). A predominant subpopulation of Gr1- CD11c- monocytes was identified in the CD11b+ population as well as subpopulations of Gr1+ CD11c- MDSCs/neutrophils, and Gr1- CD11c+ dendritc cells (middle panel). The vast majority (> 90%) of the CD11b+ Gr1- CD11c- monocytes (black line) also stained positive for the mature macrophage marker F4/80 (right panel). F4/80 staining profile of CD11b+ Gr1+ CD11c- MDSC/neutrophils (grey line, not to scale) is shown as a negative control. **Group 2:** stained with antibodies to Thy1.2 (Alexa Fluor® 488), IgMa (PE), CD4 (PE/Cy7), and CD8a (PerCP) were evaluated (left panel) for IgM+ B cells (Q1) and Thy1+ T cells (Q3). The Thy1+ population (left panel, Q3) was further evaluated (right panel) for subpopulations of CD8+ cytotoxic T cells (Q1) and CD4+ helper T cells (Q3). Analysis is shown for a pancreas obtained from a female *Ido2*-/- mouse.

**Supplemental Figure S2.** TCGA RNA expression data (N=123) derived imputed immune parameters variance across IDO2 genotypes. (A) Neutrophil to lymphocyte ratio (NLR); (B) Neutrophil to B-Cell ratio (NBR); (C) Neutrophil to T-Cell ratio (NTR); and Cytotoxic lymphocyte expression (D) show the IDO2 deficient genotype inversely correlates with neutrophil to lymphocyte ratio and positively correlates with increased cytotoxic lymphocyte expression.

**Supplemental Figure S3. *IDO2* genotype and disease-free survival in human PDAC.** The pooled TCGA-PAAD and TJUH cohorts were subjected to Kaplan-Meier survival analyses stratified by IDO2 functional genotypes as defined in Table S2. **(A)** Node-negative cases **(B)** Node Positive Cases. **(C)** Large tumor cases (>3 cm). **(D)** Small Tumor Cases (≤3 cm). **(E)** Low grade tumors. **(F)** High grade tumors.