Supplemental Table 1: **Table with antibodies and dilutions used**

Antibody	Company	Catalog Number	Species	IHC/IF-IHC	IF	WB	FACS
CCL2/MCP1	Abcam	ab25124	rabbit	1:250			
CD3	BioLegend	100222	rat				0.2 µg/1x10^6 cells
CD32	BD Pharmingen	550271	mouse				1 µg/1x10^6 cells
CD4	BioLegend	100456	rat				0.2 µg/1x10^6 cells
CD45	BioLegend	103137	rat				0.3 µg/1x10^6 cells
CD8	Abcam	ab209775	rabbit	1:500			
CD8	BioLegend	100722	rat				0.2 µg/1x10^6 cells
CK19	Santa Cruz	SC-33111	goat	1:500			
Cleaved Caspase 3	Cell Signaling Technology	9664	rabbit	1:400			
Cyclin D1	Abcam	ab16663	rabbit	1:200		1:700	
desmin	LSBioSciences	LS-C147827	rabbit			1:500	
F4/80	BioLegend	123133	rat				0.3 µg/1x10^6 cells
F4/80	BioRad	MCA497A488T	rat				0.2 tests/1x10^6 cells
F4/80	AbD Serotec	MCA497R	rat	1:200			
FXIIIA	Abcam	ab1834	mouse		1:200		
IFNγ	BioLegend	505832	rat				0.2 µg/1x10^6 cells
Ikaros	Boster Biological Technology	PB9643	rabbit	1:300			
IL-1R1	LSBioSciences	LS-C375956	rabbit	1:1000			
IL-1ra	Santa Cruz	SC-8481	goat	1:250			
iNOS	Abcam	ab3523	rabbit		1:500		
IRF4	Abcam	ab133590	rabbit			1:1000	
IRF4	antibodies online	ABIN3021306	rabbit	1:2000			
Ki67	Abcam	ab15580	rabbit	1:500			
pY641-STAT6	Abcam	ab28829	rabbit		1:200		
pY701-STAT1	Abcam	ab29045	mouse		1:250		
SMA	Abcam	ab5694	rabbit	1:200		1:1000	
Ym1	STEMCELL Technologies	60130	rabbit	1:200			
Ym1	Abcam	ab205491	rabbit				1 µg/1x10^6 cells
β-actin	Novus Biological	NB600-501H	mouse			1:2000	

Supplemental Table 1. **Antibodies and dilutions.** Antibodies used were from the following sources: Abcam (Cambridge, MA), Sigma-Aldrich (St. Louis, MO), Santa Cruz (Dallas, TX), DAKO (Carpinteria, CA), AbD Serotech (Raleigh, NC), R&D Systems (Minneapolis, MN), Invitrogen (Carlsbad, CA), BD Biosciences (San Diego, CA), LSBioSciences (Seattle, WA), STEMCELL Technologies (Vancouver, Canada), Cell Signaling Technologies (Danvers, MA), BioLegend (San Diego, CA), BD Pharmingen/ BD Biosciences (San Diego, CA), BioRad (Hercules, CA), or ThermoFisher Scientific (Waltham, MA).

Figure S1, related to Figure 1: **Treatment scheme and analyses of stroma**

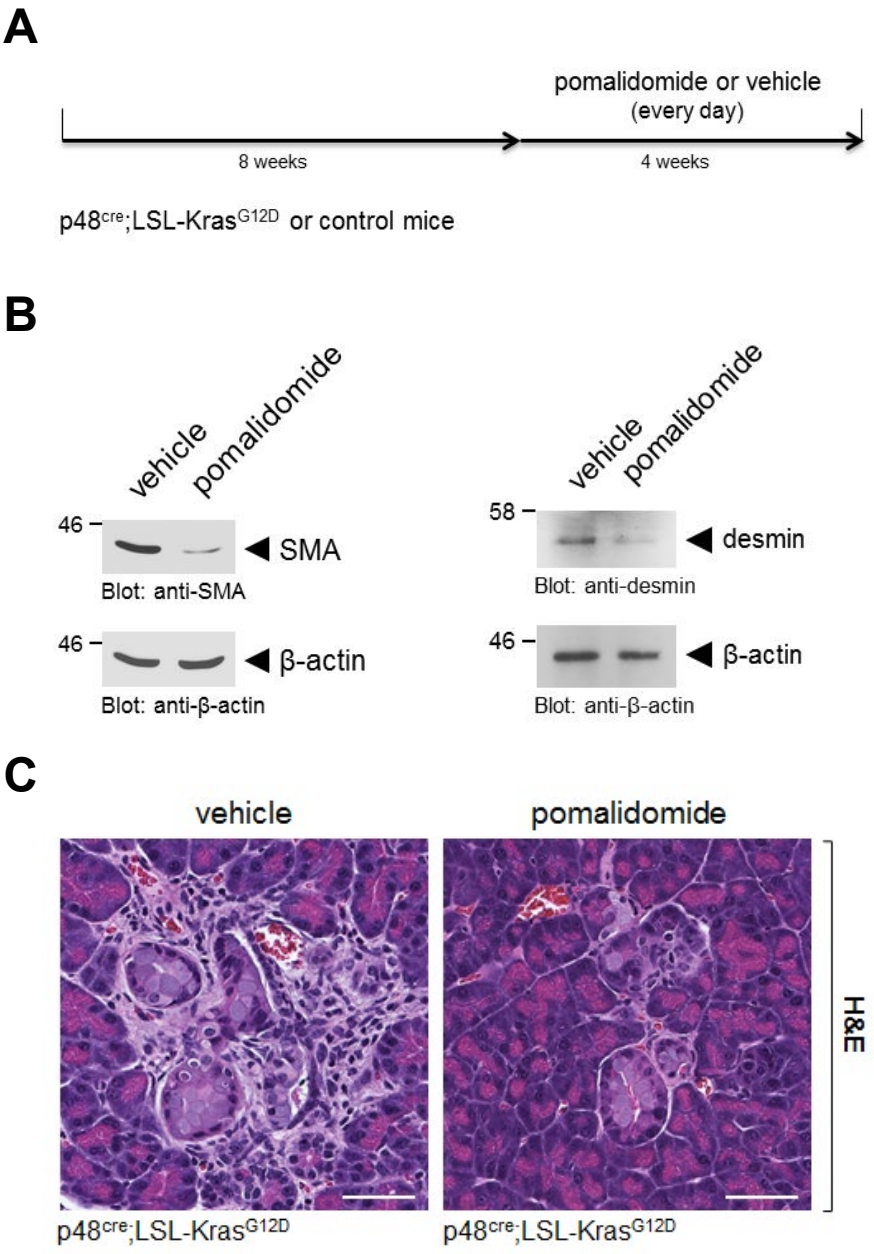

Figure S1, related to Figure 1. **A: Treatment scheme. B: Desmin expression is decreased in pancreata of KC mice treated with pomalidomide.** Tissue homogenates of pancreata of KC mice either vehicle treated (control) or treated with pomalidomide were analyzed by Western blot for expression of SMA or desmin (both markers for stellate cells) or for β-actin (loading control). **C: PanIN areas in pomalidomide treated mice show significantly-reduced surrounding stroma.** H&E staining of KC mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. Shown are representative PanIN areas. The bar indicates 50 μm.

Figure S2, related to Figure 2: **Additional analyses of cell death and cell proliferation**

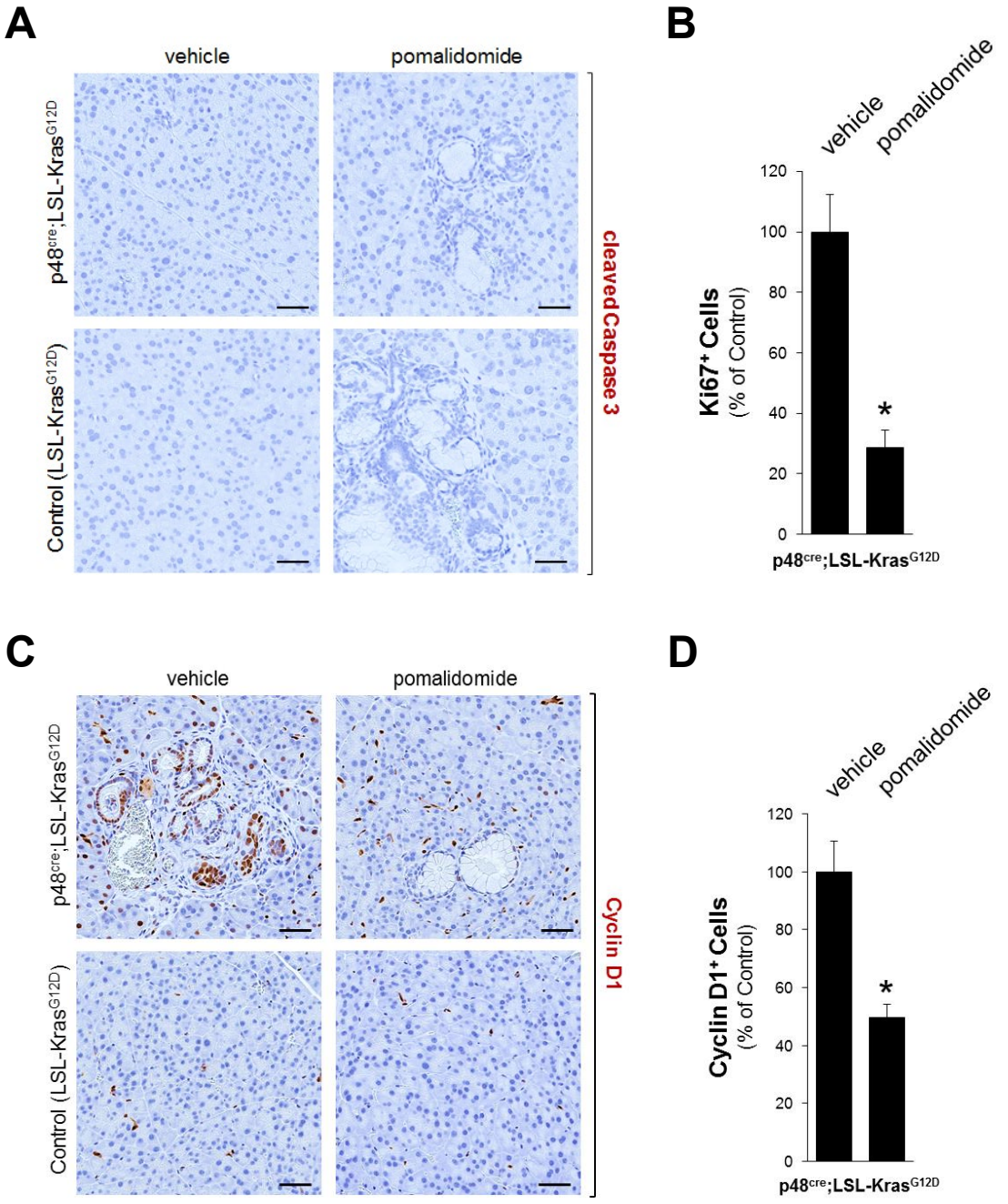

Figure S2, related to Figure 2. **A: Pomalidomide does not induce cell death in lesion areas.** IHC staining of KC or control (LSL-Kras^{G12D}) mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. Shown are representative areas of tissue slides stained (IHC) for cleaved caspase 3. The bar represents 50 µm. **B-D: Pomalidomide reduces cell proliferation in lesion areas. B:** Quantification of Ki67 positive cells. IHC stained samples of n=3 mice from each treatment group were analyzed. The asterisk indicates statistical significance ($p<0.05$). **C:** Representative IHC staining of pancreatic abnormal areas for Cyclin D1 as marker for proliferating cells. Representative areas are shown in B. The scale bar indicates 50 µm. **D:** Quantification of Cyclin D1 positive cells. IHC stained samples of n=3 mice from each treatment group were analyzed. The asterisk indicates statistical significance ($p<0.05$).

Figure S3, related to Figure 3: **Presence of Ym1+ macrophage and IL-13 in PanIN areas**

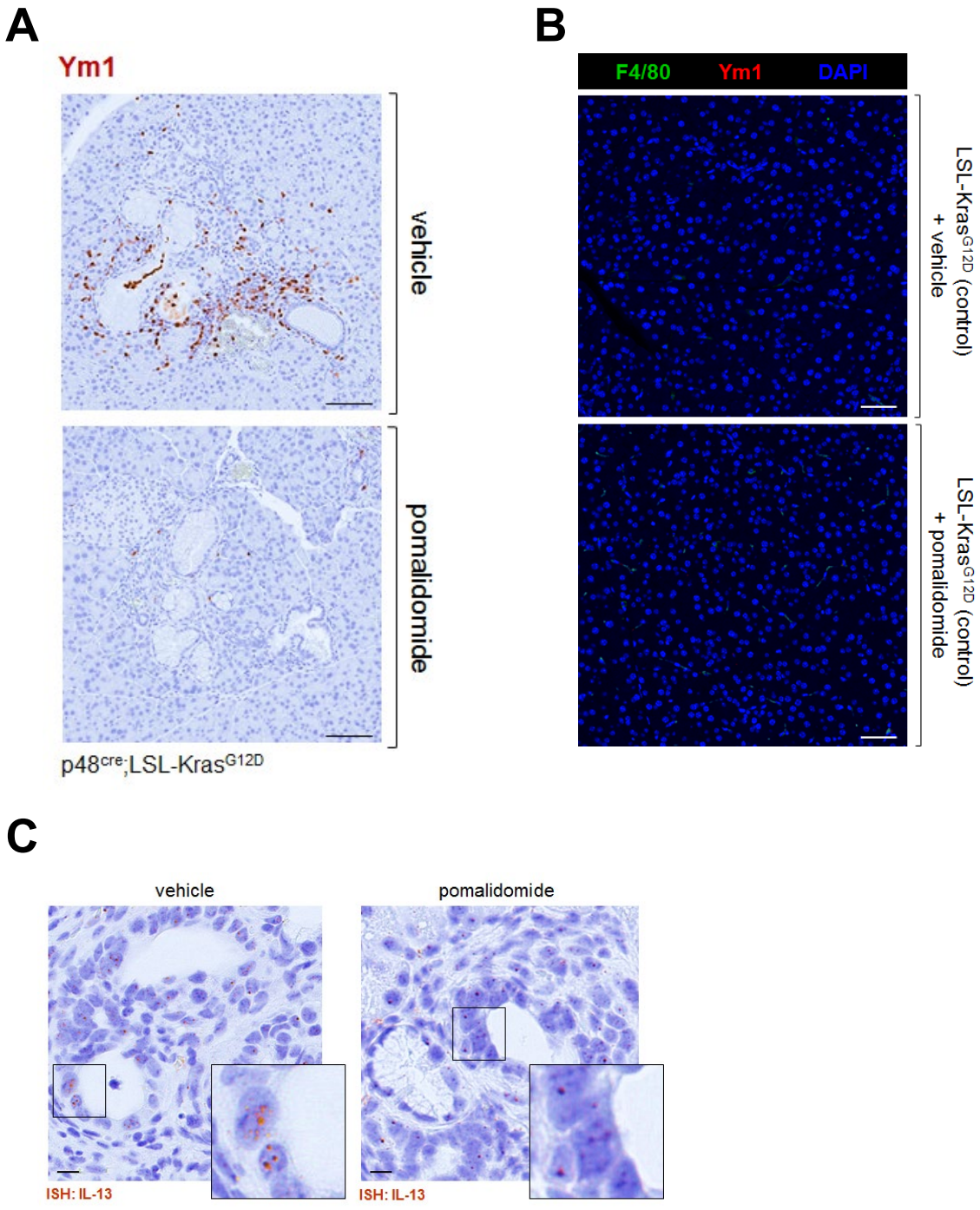

Figure S3, related to Figure 3. **A: Treatment with pomalidomide decreases Ym1+ cells in PanIN areas.** IHC staining of KC mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. Shown are representative areas of tissue slides stained (IHC) for Ym1. The bar represents 50 µm. **B: Controls for Figure 3C.** Shown is the composite for LSL-Kras^{G12D} (control) mice either treated with vehicle or pomalidomide. The bar indicates 50 µm. **C: Pomalidomide does not affect presence/production of IL-13 at PanIN lesions.** Shown is a representative *in situ* hybridization (ISH) for IL-13 mRNA (brown dots) in KC mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. The bar indicates 10 µm.

Figure S4, related to Figure 4: **Additional data on the role of IRF4 in macrophage polarization**

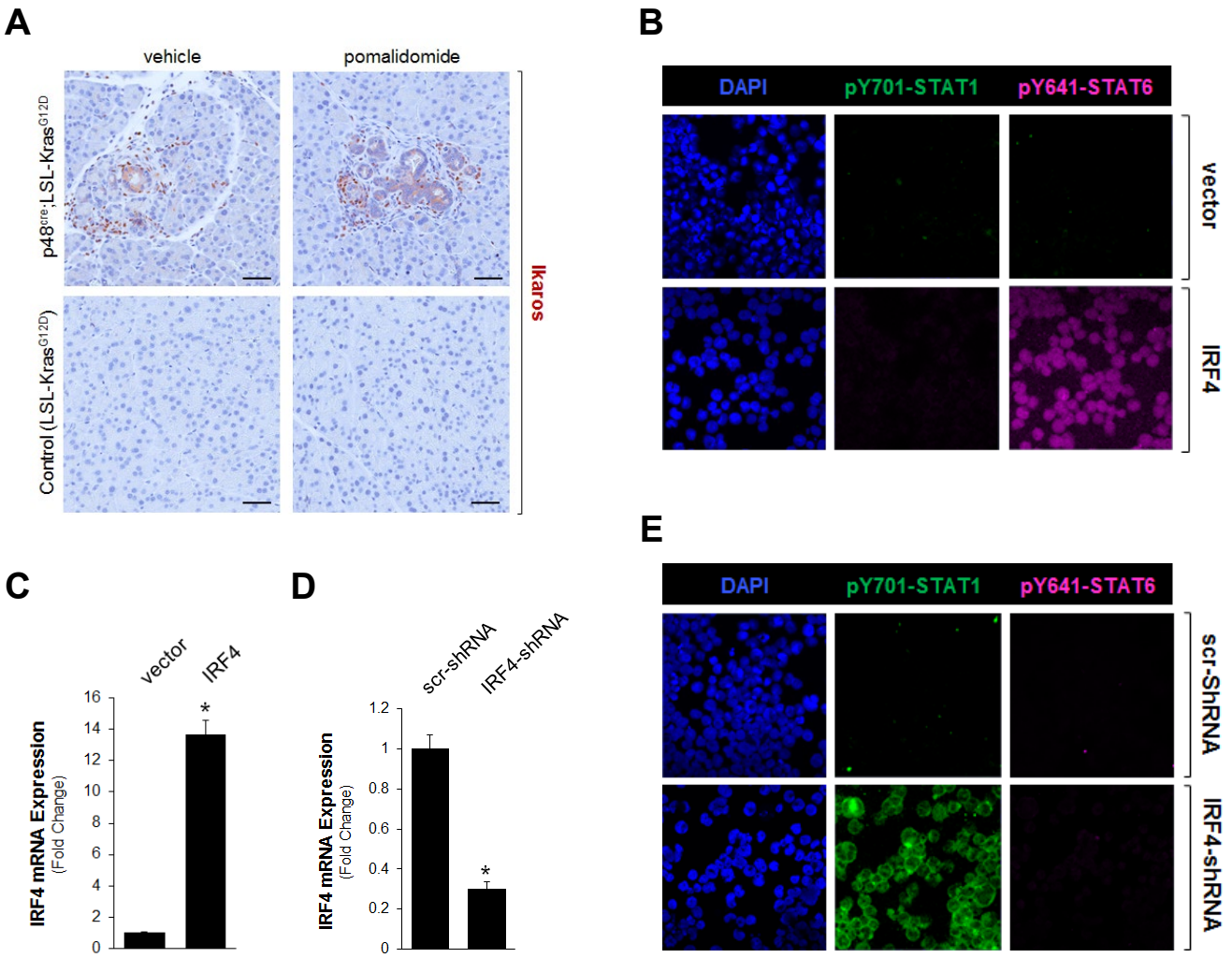

Figure S4, related to Figure 4. **A: Pomalidomide does not affect the levels of Ikaros at lesion areas.** IHC staining of KC or control (LSL-Kras^{G12D}) mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. Shown are representative areas of tissue slides stained (IHC) for Ikaros. The bar indicates 50 μm. **C, D: Controls for IRF4 expression for Figures 4C and 4D.** Shown are quantitative RT-PCRs for IRF4 mRNA. The asterisk indicates statistical significance. **B, E: IRF4 levels drive macrophage polarization.** U937 cells were transfected with control vector or IRF4 (B) or with control or IRF4-shRNA (E) as described in Figs. 4C, 4D and subjected to IF analysis for expression of pY701-STAT1 (M1 marker) or pY641-STAT6 (M2 marker) combined with DAPI staining.

Figure S5, related to Figure 5: **Presence of macrophage-secreted factors and T cells**

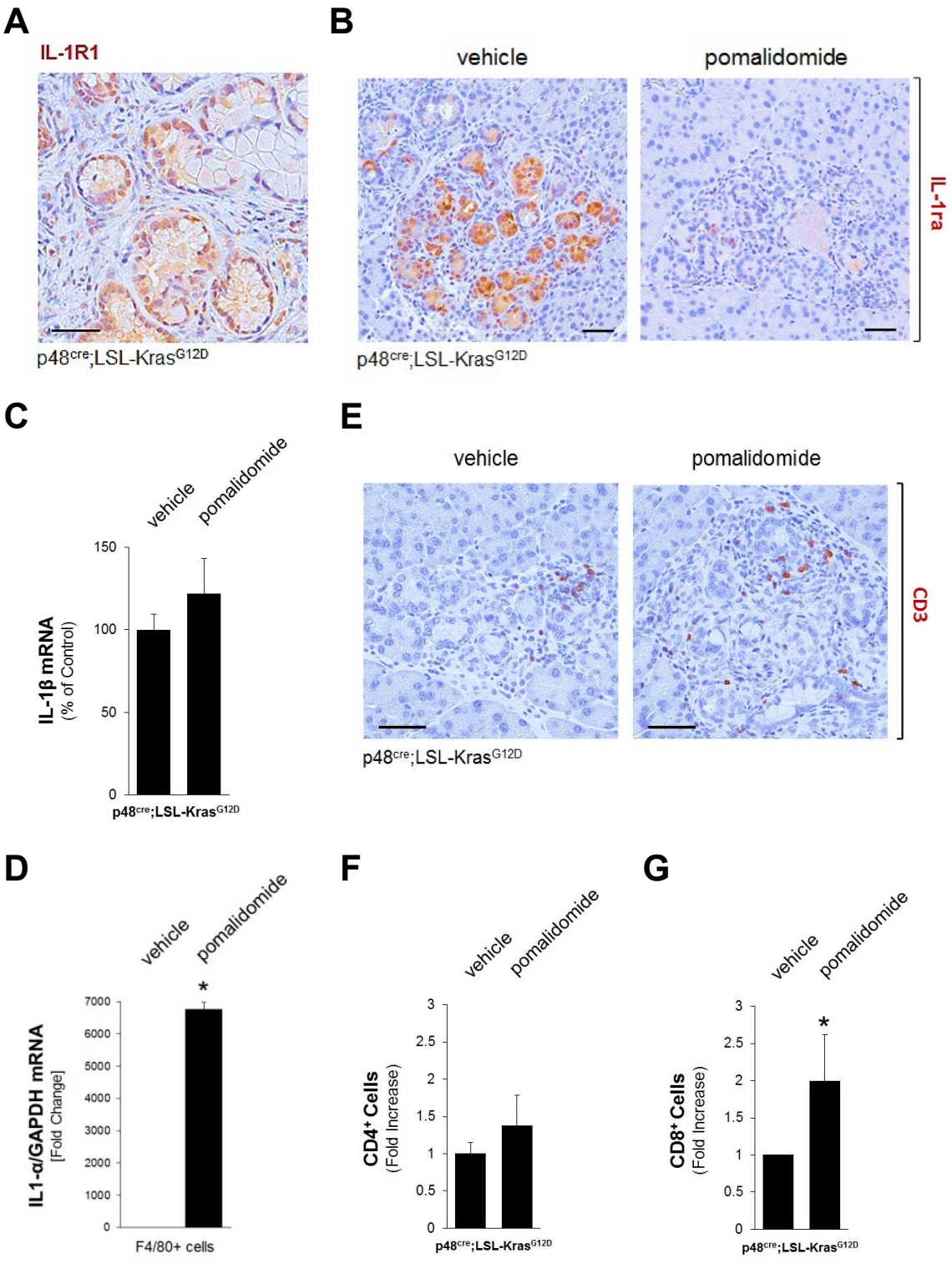

Figure S5, related to Figure 5. **A: IL-1R expression in abnormal pancreatic areas of KC mice.** Shown is a representative area stained (IHC) for IL-1R. The bar represents 50 µm**. B:** Immunohistochemical analysis of IL-1ra expression in pancreata of vehicle or pomalidomide treated mice. Shown are representative areas. The scale bar indicates 50 µm. **C:** Quantification of cells positive for IL-1β mRNA (ISH) in pancreata of n=3 mice per experimental group. **D: Q-PCR (after FACS) for IL-1α expression in pancreatic F4/80+ cells. E: Treatment with pomalidomide increases the presence of CD3+ cells in pancreatic lesion areas.** IHC staining of KC mice either vehicle treated (control) or treated with pomalidomide, as indicated in Fig. S1A. Shown are representative areas of tissue slides stained (IHC) for CD3. The bar represents 50 µm. **F, G:** Quantifications of CD4+ (**F**) and CD8+ (**G**) cells after IHC analyses similar as performed in (**E**).

Figure S6, related to Figure 6: **Treatment scheme and analyses of presence of immune cells**

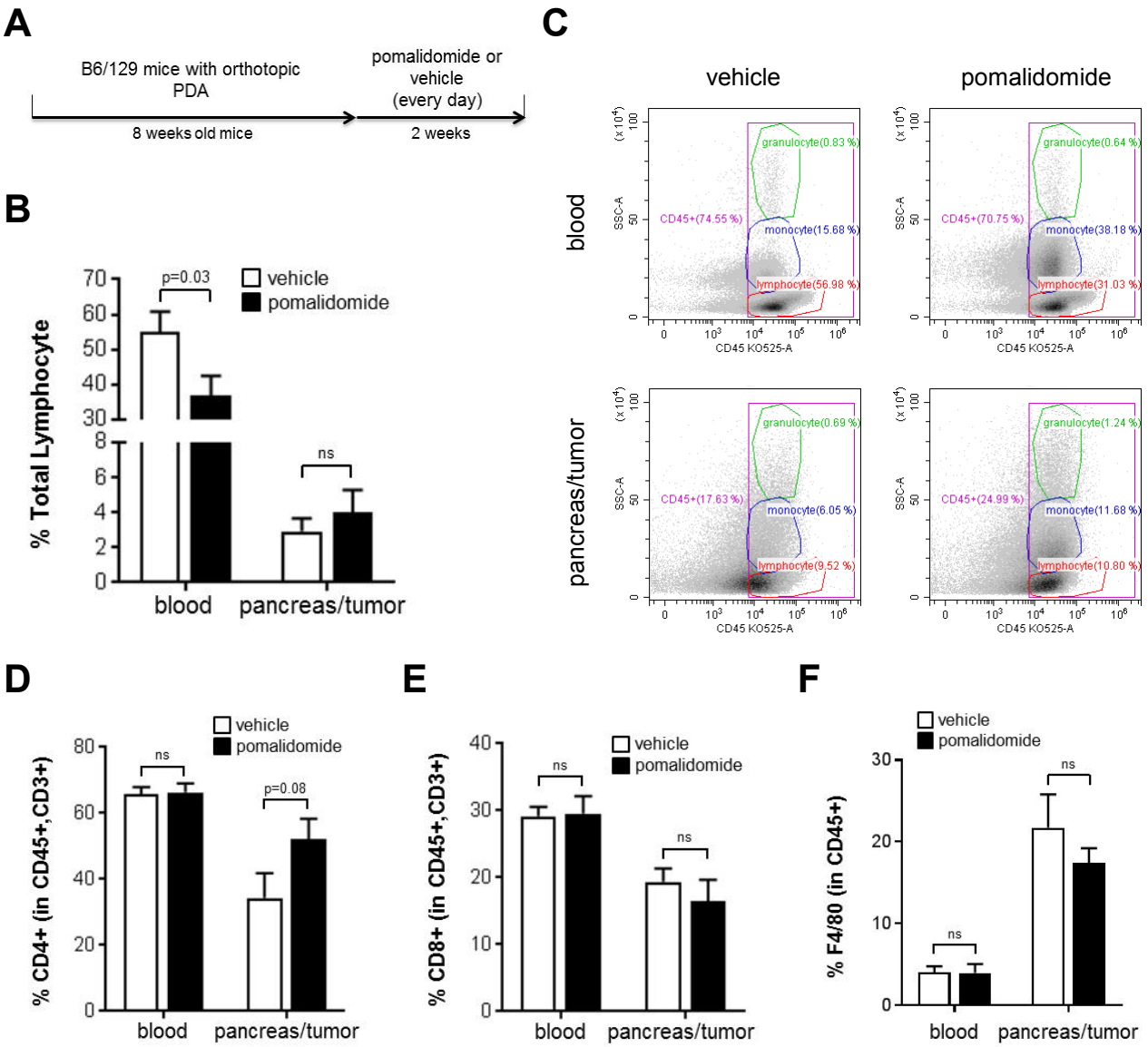

Figure S6, related to Figure 6. **A: Treatment Scheme.** After orthotopic implantation of KPC1 tumor cells and PSC and tumor formation, 8 weeks old mice were treated with vehicle or pomalidomide for two weeks, as indicated. **B, C: Total lymphocytes in blood and pancreas/tumor tissue in mice with orthotopic PDA.** Flow cytometry of blood or pancreas/tumor tissue from control or pomalidomide treated mice (n=3 per treatment group) to determine % total lymphocytes. Gating is based on the CD45 scatter plot shown in **C**. **D, E: CD4+ and CD8+ T cell composition in blood or pancreas/tumor samples before and after treatment.** Flow cytometry of blood or pancreas/tumor tissue from control or pomalidomide treated (n=3 per treatment group) mice to determine CD4+and CD8+ T cells. Gating is based on CD4+ or CD8+ cells in the total CD45+,CD3+ population. **F: Macrophages in blood or pancreas/tumor samples before and after treatment.** Flow cytometry of blood or pancreas/tumor tissue from control or pomalidomide treated (n=3 per treatment group) mice to determine the presence of macrophages. Gating is based on F4/80 positive cells in the total CD45+ population.

Figure S7, related to Figures 1-6: **Blood counts and coagulation profile**

A

Group	Neutrophil/µl	WBC (K/µl)	RBC (M/µl)	HGB (g/dl)	Lymphocyte/µl	HCT (%)	Monocyte/µl	Eosinophil/µl	MCV (fl)	Basophil/µl	MCH (pg)	MCHC (g/dl)
control	1421	6.8	9.88	14.9	4740	45.2	354	279	46	7	15.1	33
control	1725	7.5	9.5	14.6	5048	45	525	203	47	0	15.4	32.4
control	6510	15	8.5	12.5	6420	39.9	1710	345	47	15	14.7	31.3
control	1990	9.3	9.28	14.7	6501	45.6	605	195	49	9	15.8	32.2
pomalidomide	3070	10	8.83	12.9	5780	40	680	460	45	10	14.6	32.3
pomalidomide	956	7.9	9.5	14.5	6115	45.5	600	221	48	8	15.3	31.9
pomalidomide	1817	7.9	9.46	14.5	5380	44.8	577	119	47	8	15.3	32.4
pomalidomide	3236	11.6	8.88	13.2	7250	41.2	696	406	46	12	14.9	32

B

Group	Neutrophil/µl	WBC (K/µl)	RBC (M/µl)	HGB (g/dl)	Lymphocyte/µl	HCT (%)	Monocyte/µl	Eosinophil/µl	MCV (fl)	Basophil/µl	MCH (pg)	MCHC (g/dl)
control	1271	7.8	9.95	15.2	5749	50.7	601	179	51	0	15.3	30
control	1785	10.5	10.42	16.2	7455	51.7	1260	0	50	0	15.5	31.3
control	1643	10.6	9.55	14.1	8501	47.1	350	106	49	0	14.8	29.9
pomalidomide	1184	8.9	10.01	15	7209	49	356	142	49	9	15	30.6
pomalidomide	835	7.8	9.2	13.6	6568	44.8	281	117	49	0	14.8	30.4
pomalidomide	963	9	9.36	14.6	7254	48.6	630	144	52	9	15.6	30

C

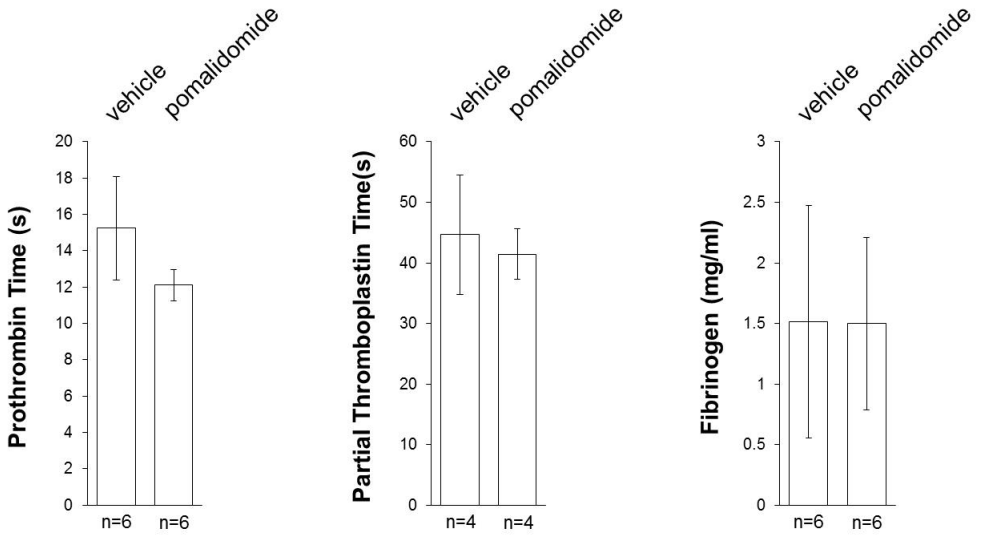

Figure S6, related to Figures 1-6. **A, B: Complete blood count (CBC) of KC (A) or syngeneic mice (B) from indicated treatment groups.** Mouse blood from n=4 mice (KC, **A**) or n=3 mice (syngeneic, **B**) per treatment group was collected by cardiac puncture and stored in EDTA-treated collection tubes. CBC analyses were performed by IDEXX Laboratories (Westbrook, ME). Abbreviations/definitions: WBC, white blood cell; RBC, red blood cell; HBG, hemoglobin; HCT, hematocrit; MCV, average volume of a red blood cell; MCH, average amount of hemoglobin in the average red blood cell; MCHC, mean corpuscular hemoglobin concentration. Other CBC criteria/cells such as band/µl, nucleated RBC/100 WBC, poikilocytosis, Heinz bodies, metamyelocytes, myelocytes or promyelocytes were determined as "none seen" in all samples. The platelet estimate was determined as "adequate" in all samples, and polychromasia and anisocytosis were "slight/moderate" in all samples. **C: Coagulation Profile for syngeneic mice.** The coagulation profile (Prothrombin time, Partial Thromboplastin time, Fibrinogen levels) for indicated numbers of mice either vehicle treated or control treated were analyzed. Analyses were performed by IDEXX Laboratories.