

Supplemental Data

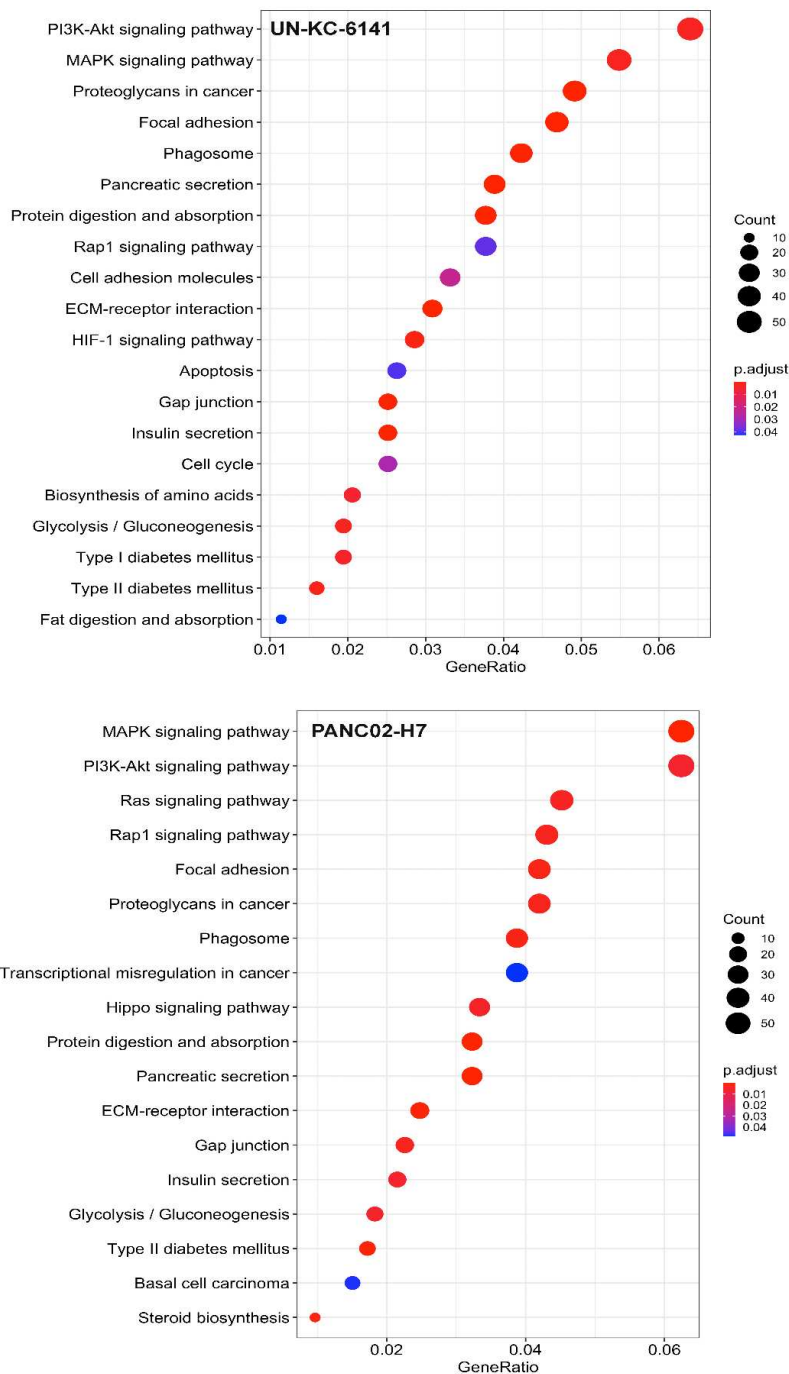


Figure S1. KEGG pathway enrichment in pancreatic carcinoma in vivo. The differentially expressed genes between normal pancreas and the two orthotopic pancreatic tumors were analyzed for pathway enrichment using R package clusterProfiler. Benjamini-Hochberg (BH)-adjusted p-value <0.05) was used as cutoff value.

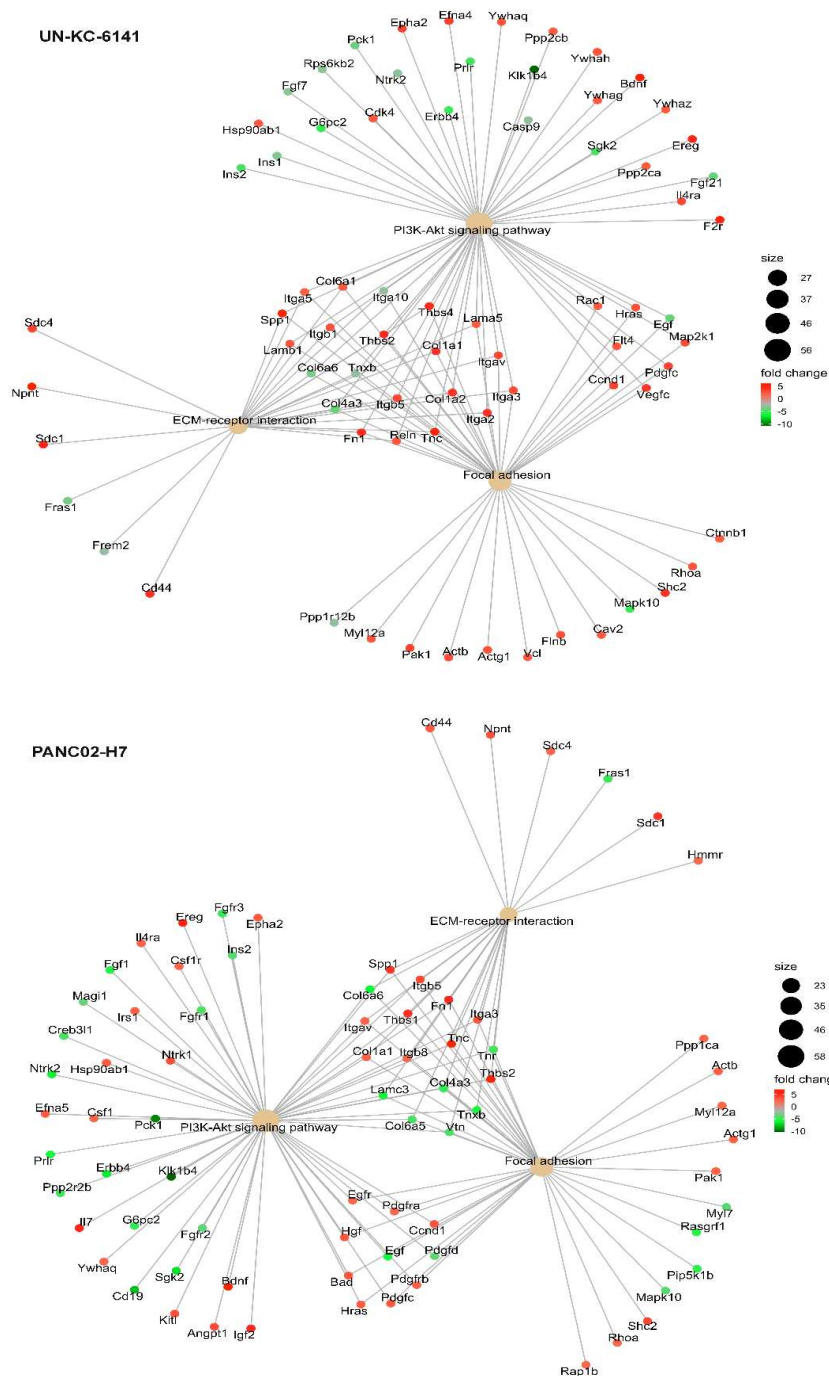


Figure S2. Differentially expressed genes in KEGG pathway. The differentially expressed genes between normal pancreas and the two orthotopic pancreatic tumors in the three indicated pathways are shown in cnet plots generated by clusterProfiler.

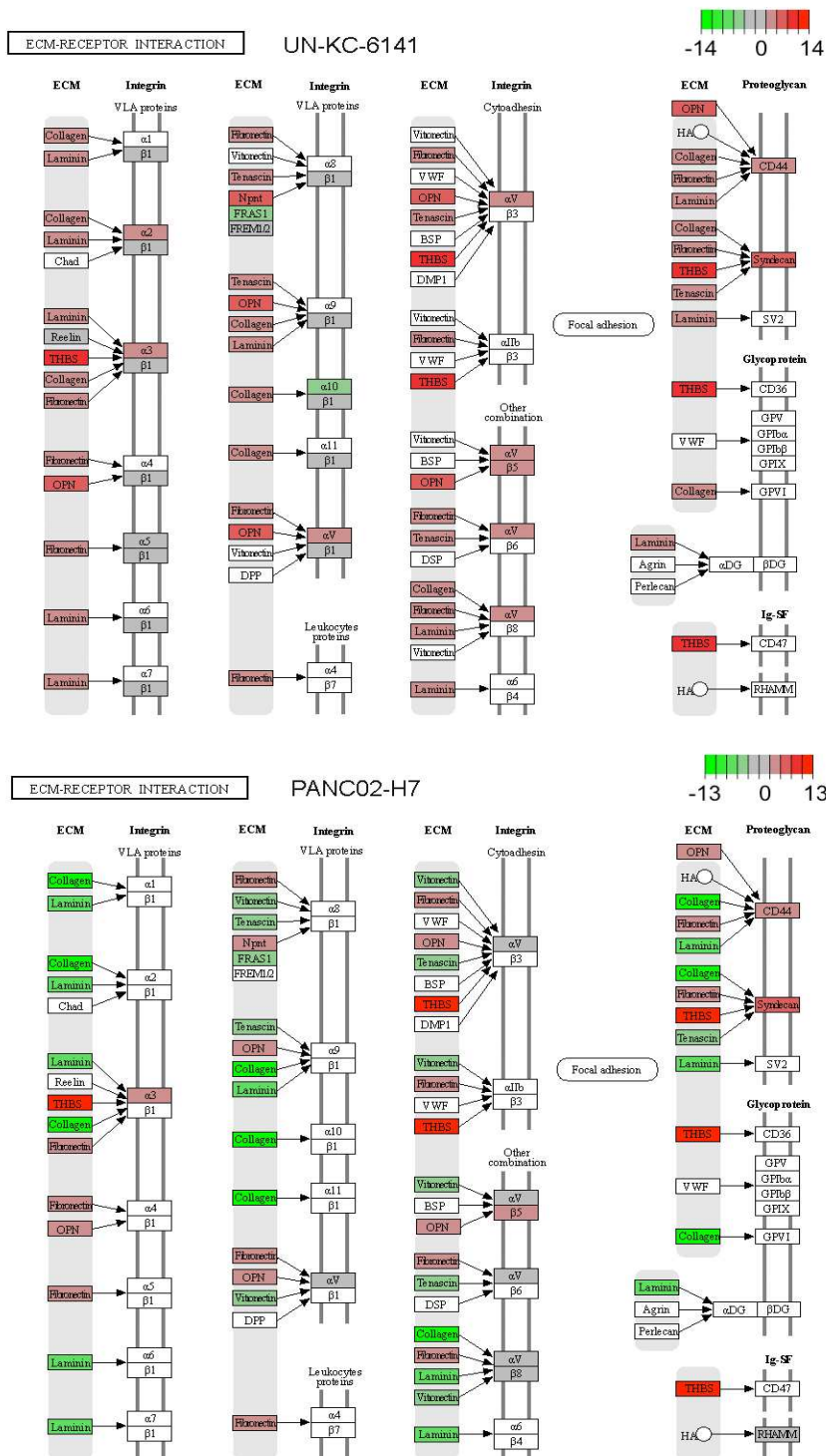


Figure S3. ECM-receptor interaction map. The differentially expressed genes were mapped to their respective ligands or receptors using R package pathview. Red color indicates up-regulated genes in tumors and green color indicates down-regulated genes in tumors.

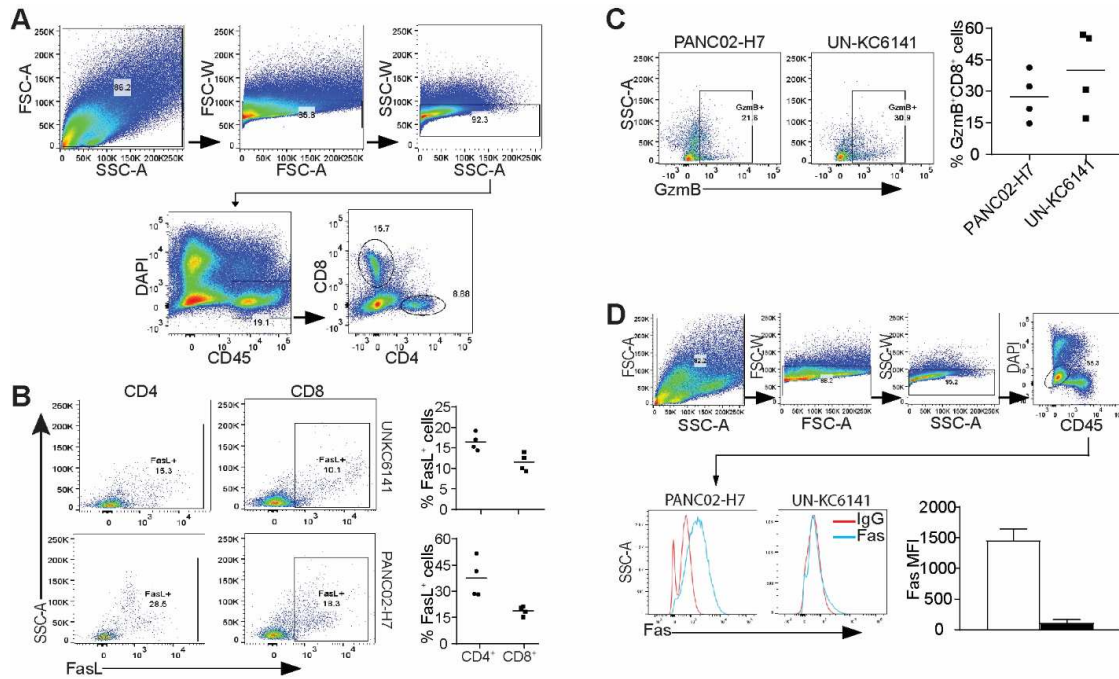


Figure S4. T cell effector and tumor death receptor expression in pancreatic carcinoma. A. The orthotopic UN-KC-6141 and PANC02-H7 tumors were collected from tumor-bearing mice and processed for analysis of tumor cells and tumor-infiltrating immune cells. Shown is gating strategy. **B.** FasL expression in T cells as gated in A was analyzed by flow cytometry. The % FasL⁺ cells were quantified and presented at the right. **C.** Gzmb expression in tumor-infiltrating CD8⁺ T cells was analyzed and quantified. **D.** Live tumor cells were gated and analyzed for Fas expression level in the two tumors. The Fas MFI is quantified at the right panel.

Table S1. Normal human pancreas

Patient	Tissue	Age	Race	Sex	Patient diagnosis	Treatment prior to tissue resection
15-01-A072d-1	Normal Pancreas	40	Black	Female	Cholangiocarcinoma	None
15-01-A076c-1	Normal Pancreas	62	White	Female	Neuroendocrine tumor	None
15-02-A084a-b	Normal Pancreas	22	Black	Male	Adrenal cortical carcinoma	None
15-03-A038c-1	Normal Pancreas	73	White	Male	Adenocarcinoma of pancreas	None
15-05-A033d-1	Normal Pancreas	63	Black	Male	Adenocarcinoma of pancreas	None

Table S2. Human pancreatic tumor tissues

Patient	Diagnosis of Samples	Age	Race	Sex	Treatment prior to tumor resection
15-01-A016c-1	Adenocarcinoma of pancreas	70	White	Female	None
15-02-A095i-1	Adenocarcinoma of pancreas	74	White	Male	None
15-05-A070a-1	Adenocarcinoma of pancreas	69	White	Female	None
15-05-A085e	Adenocarcinoma of pancreas	70	White	Female	None
15-08-A037d-1	Adenocarcinoma of pancreas	53	White	Male	None

Table S3. Patient survival and OPN expression level

Patient	Days	Status	OPN Expression	Cutoff
TCGA-3A-A9IR	1542	Alive	29.95	Low
TCGA-FB-AAPP	485	Dead	202.4	Low
TCGA-3A-A9IS	998	Alive	237.62	Low
TCGA-3A-A9IN	2084	Alive	373.56	Low
TCGA-US-A776	1216	Alive	376.78	Low
TCGA-FB-AAPU	381	Dead	553.8	Low
TCGA-2J-AABA	607	Dead	1021.45	Low
TCGA-3A-A9IV	1103	Alive	1071.98	Low
TCGA-HZ-7289	661	Dead	1106.12	Low
TCGA-2L-AAQE	684	Dead	1178.87	Low
TCGA-3A-A9IO	1942	Alive	1196.95	Low
TCGA-3A-A9IJ	1854	Alive	1211.86	Low
TCGA-Z5-AAPL	467	Alive	1747.58	Low
TCGA-3A-A9I7	1323	Alive	1780.22	Low
TCGA-FB-AAQ0	473	Dead	1982.29	Low
TCGA-HZ-A49I	308	Dead	1987.07	Low
TCGA-2J-AAB8	80	Alive	2047.47	Low
TCGA-HZ-8637	517	Dead	2324.37	Low
TCGA-S4-A8RM	737	Alive	2338.05	Low
TCGA-3A-A9IL	2741	Alive	2357.64	Low
TCGA-IB-AAUR	338	Alive	2394.05	Low
TCGA-XD-AAUH	395	Alive	2513.79	Low
TCGA-LB-A7SX	393	Dead	2564.77	Low
TCGA-3E-AAAZ	2182	Dead	2703.07	Low
TCGA-IB-AAUP	431	Alive	2737.21	Low
TCGA-XN-A8T5	720	Alive	2892.13	Low
TCGA-IB-A5ST	635	Alive	2998.69	Low
TCGA-Q3-AA2A	95	Alive	3041.82	Low
TCGA-HZ-A4BH	194	Alive	3250.78	Low
TCGA-FB-A7DR	353	Dead	3271.69	Low
TCGA-2J-AABP	463	Alive	3283.53	Low
TCGA-F2-6879	334	Dead	3904.59	Low
TCGA-HZ-A4BK	657	Alive	4019.77	Low
TCGA-2J-AABI	969	Alive	4062.77	Low
TCGA-HZ-8519	454	Alive	4161.49	Low
TCGA-US-A77G	12	Dead	4324.97	Low
TCGA-HZ-7925	614	Dead	4511.45	Low
TCGA-IB-A7M4	483	Alive	4636.06	Low
TCGA-YY-A8LH	2016	Alive	4688.35	Low
TCGA-L1-A7W4	278	Dead	4776.67	Low
TCGA-XD-AAUG	420	Alive	4908.11	Low
TCGA-IB-7897	486	Dead	5229.49	Low
TCGA-HV-A7OL	252	Alive	5260.63	Low
TCGA-2J-AABU	277	Dead	5587.34	Low
TCGA-IB-7888	1332	Dead	5741.88	Low
TCGA-HV-A5A6	2036	Dead	5768.74	Low
TCGA-HZ-7924	840	Alive	5809.23	Low
TCGA-HV-AA8X	532	Dead	6011.24	Low
TCGA-FB-AAQ2	153	Dead	6094.93	Low
TCGA-HZ-A8P1	7	Alive	6179.04	Low
TCGA-FB-AAQ6	244	Dead	6257.28	Low
TCGA-H8-A6C1	671	Alive	6317.89	Low
TCGA-IB-7647	666	Dead	6349.45	Low
TCGA-YH-A8SY	388	Alive	6507.59	Low
TCGA-2J-AABO	440	Alive	6709.94	Low
TCGA-HZ-A49H	491	Alive	7039.62	Low
TCGA-HZ-8001	706	Alive	7123.93	Low
TCGA-IB-7887	110	Dead	7208.2	Low
TCGA-M8-A5N4	584	Alive	7436.53	Low
TCGA-FB-A5VM	498	Dead	7870.11	Low
TCGA-HZ-A77Q	33	Alive	7876.62	Low

TCGA-HV-A5A4	232	Alive	7928	Low
TCGA-IB-AAUV	404	Alive	8199.59	Low
TCGA-HZ-A77P	330	Alive	8412.58	Low
TCGA-IB-7645	1502	Dead	8462.79	Low
TCGA-IB-7886	123	Dead	8649.31	Low
TCGA-F2-A8YN	517	Alive	8732.08	Low
TCGA-IB-A5SP	482	Alive	9206.7	Low
TCGA-IB-7644	394	Dead	9437.12	Low
TCGA-3A-A9IB	224	Dead	9727.7	Low
TCGA-IB-AAUM	8	Alive	9736.92	High
TCGA-2J-AAB1	66	Dead	9841.95	High
TCGA-Q3-A5QY	416	Alive	9908.15	High
TCGA-IB-8127	522	Alive	10156.83	High
TCGA-HZ-7920	236	Dead	10413.23	High
TCGA-OE-A75W	267	Dead	11076.46	High
TCGA-HZ-8317	378	Dead	11114.06	High
TCGA-HZ-A9TJ	603	Alive	11400.16	High
TCGA-US-A779	511	Dead	12075.49	High
TCGA-2L-AAQA	143	Dead	12522.02	High
TCGA-2J-AABT	319	Alive	12588.24	High
TCGA-2J-AABE	676	Alive	12628.33	High
TCGA-2J-AAB6	293	Dead	12734.5	High
TCGA-3A-A9IC	738	Dead	12843.46	High
TCGA-F2-6880	295	Alive	12877.57	High
TCGA-F2-A44G	233	Dead	13081.68	High
TCGA-IB-7654	476	Dead	13128.45	High
TCGA-FB-A545	732	Dead	13270.25	High
TCGA-2L-AAQJ	394	Dead	13295.54	High
TCGA-XD-AAUL	498	Alive	13317.26	High
TCGA-IB-7885	1257	Alive	13350.34	High
TCGA-IB-A5SQ	219	Dead	13569.78	High
TCGA-HZ-8315	299	Dead	14132.15	High
TCGA-IB-8126	462	Alive	14370.9	High
TCGA-H6-8124	392	Alive	14461.94	High
TCGA-HZ-7919	593	Dead	14492.59	High
TCGA-RB-A7B8	466	Dead	15006.57	High
TCGA-IB-AAUN	144	Dead	15283.87	High
TCGA-IB-AAUS	225	Alive	15290.54	High
TCGA-S4-A8RP	702	Dead	15678.67	High
TCGA-HZ-8003	596	Dead	15751.44	High
TCGA-IB-A5SO	365	Dead	15827.59	High
TCGA-FB-A78T	375	Dead	16106.12	High
TCGA-IB-AAUO	239	Dead	16143.88	High
TCGA-2J-AABH	1287	Alive	17129.36	High
TCGA-2J-AABF	691	Dead	17151.77	High
TCGA-IB-A7LX	250	Dead	17863.21	High
TCGA-FB-AAPZ	716	Alive	18144.1	High
TCGA-HZ-7922	4	Alive	18801.71	High
TCGA-F2-A44H	586	Alive	19079.42	High
TCGA-3A-A9IX	1037	Alive	19274.32	High
TCGA-HZ-7926	518	Dead	19388.49	High
TCGA-YB-A89D	350	Alive	19501.03	High
TCGA-FB-AAPS	228	Alive	20690.34	High
TCGA-US-A774	695	Dead	20886.74	High
TCGA-PZ-A5RE	470	Dead	21074.61	High
TCGA-S4-A8RO	525	Alive	21572.98	High
TCGA-3A-A9J0	743	Alive	21613.94	High
TCGA-US-A77E	430	Dead	21795.63	High
TCGA-IB-AAUU	245	Alive	21932.25	High
TCGA-XD-AAUI	366	Dead	22054.98	High
TCGA-IB-7646	145	Dead	22161.93	High
TCGA-HV-A5A3	128	Dead	22572.62	High
TCGA-RB-AA9M	286	Alive	23967.81	High

TCGA-3A-A9IZ	308	Dead	24070.63	High
TCGA-HZ-7923	314	Alive	24675.28	High
TCGA-3A-A9IH	1021	Alive	24914.14	High
TCGA-XN-A8T3	951	Alive	24935.13	High
TCGA-LB-A8F3	379	Alive	25001.02	High
TCGA-FB-AAPY	1059	Dead	25192.31	High
TCGA-3A-A9IU	458	Dead	25219.68	High
TCGA-HZ-A770	160	Dead	25311.31	High
TCGA-FB-A4P6	767	Alive	25506.81	High
TCGA-H6-A45N	421	Dead	25839.44	High
TCGA-US-A77J	568	Dead	26733.86	High
TCGA-IB-7889	481	Dead	26952.62	High
TCGA-2L-AAQL	292	Dead	27025.79	High
TCGA-3E-AAAY	2285	Alive	27438.32	High
TCGA-IB-A5SS	460	Dead	27680.8	High
TCGA-HZ-7918	969	Alive	27937.01	High
TCGA-2J-AABK	484	Alive	28105.33	High
TCGA-F2-7273	592	Dead	28580.44	High
TCGA-FB-A4P5	179	Dead	29006.72	High
TCGA-2L-AAQM	1383	Alive	29088.43	High
TCGA-HZ-8636	545	Dead	29496.46	High
TCGA-IB-7651	603	Dead	29782.79	High
TCGA-IB-AAUQ	183	Dead	31128.83	High
TCGA-HZ-8002	366	Dead	32323.35	High
TCGA-F2-A7TX	95	Dead	33146	High
TCGA-FB-AAPQ	1130	Dead	33150.55	High
TCGA-IB-7652	1116	Alive	33716.41	High
TCGA-RL-AAAS	9	Alive	33788.32	High
TCGA-2J-AABR	438	Alive	35384.04	High
TCGA-IB-7893	117	Dead	35603.45	High
TCGA-2L-AAQI	103	Dead	39661.07	High
TCGA-F2-7276	216	Dead	39898.19	High
TCGA-IB-AAUW	230	Dead	40794.34	High
TCGA-IB-A6UG	41	Dead	42115.01	High
TCGA-3A-A9I9	634	Dead	42269.69	High
TCGA-IB-7891	913	Dead	44550.66	High
TCGA-HZ-8005	120	Dead	44715.83	High
TCGA-2J-AABV	652	Dead	46651.97	High
TCGA-LB-A9Q5	313	Dead	46887.42	High
TCGA-FB-AAQ3	31	Dead	47218.68	High
TCGA-2J-AAB9	627	Dead	47747.05	High
TCGA-IB-7890	598	Dead	49693.05	High
TCGA-IB-A6UF	666	Alive	53108.57	High
TCGA-2J-AAB4	729	Alive	54838.38	High
TCGA-IB-7649	467	Dead	61621.51	High
TCGA-IB-AAUT	287	Alive	63261.96	High
TCGA-HZ-A49G	660	Alive	67481.4	High
TCGA-FB-AAQ1	123	Dead	68175.37	High
TCGA-HV-AA8V	920	Alive	70061.59	High
TCGA-HV-A5A5	289	Alive	73456.38	High
TCGA-3A-A9I5	1794	Alive	96867.35	High

Table S4. PCR primers

mSPP1-F1	GCCTGTTTGGCATTGCCTCCTC
mSPP1-B1	CACAGCATTCTGTGGCGCAAGG
mCD44-F	ACTCAAGTGCGAACCAGGACAG
mCD44-B	GCTTTTCTTCTGCCACACC
mSpp1-ChIP-1F	GAGGAAACCAGCCAAGGTAAGC
mSpp1-ChIP-1B	CAAAAAGACCAGAACAGCACGAG
mSpp1-ChIP-2F	AGGGTCTGAAAGTTCTGCCGAG
mSpp1-ChIP-2B	GGGGATGAAAGGTATGGATTCTCC
mSpp1-ChIP3-F	AGCAGGGTTTGGCAAGTAGCAC
mSpp1-ChIP3-B	TCCCGAAATGGAGAACACAGGC
mSpp1-ChIP-4F	TTAACCCCAAGTGGCTACACG
mSpp1-ChIP-4B	TCATGTTGAAGTCCCCTTAAAGTAG

Table S5. Flow cytometry antibodies

Antibody	Source	Clone	Cat Number	Application
PE-Cy7 anti-mouse CD45.2	Biolegend	104	109830	Flow Cytometry
FITC anti-mouse CD4	Biolegend	GK1.5	100406	Flow Cytometry
PerCP anti-mouse CD8	Biolegend	53-6.7	100732	Flow Cytometry
APC anti-mouse PD-1	Biolegend	29F.1A12	135210	Flow Cytometry
PE anti-mouse FasL	Biolegend	Kay-10	106805	Flow Cytometry
FITC anti-human/mouse CD11b	Biolegend	M1/70	101206	Flow Cytometry
PerCP anti-mouse Gr1	Biolegend	RB6-8C5	108426	Flow Cytometry
APC anti-mouse PD-L1	Biolegend	10F.9G2	124312	Flow Cytometry
AF700 anti-mouse Ly6G	Biolegend	1A8	127622	Flow Cytometry
PerCP anti-mouse Ly6C	Biolegend	HK1.4	128028	Flow Cytometry
PE-Cy7 anti-mouse F4/80	Biolegend	BM8	123114	Flow Cytometry
AF700 anti-mouse CD206	Biolegend	C068C2	141734	Flow Cytometry
FITC anti-mouse Fas	BD Pharmingen	Jo2	554257	Flow Cytometry
PE anti-mouse OPN	R&D Systems	N/A	IC808P	Flow Cytometry
Pacific Blue anti-human/mouse GzmB	Biolegend	GB11	515408	Flow Cytometry
FITC mouse IgG	Biolegend	Poly4060	406001	Flow Cytometry
APC Armenian Hamster IgG	Biolegend	HTK888	400912	Flow Cytometry

Table S6: Two-factor ANOVA results of WDR5-47 and anti-PD-1 immunotherapy on tumor weight and size

Outcome	Effect in Model	Level of WDR5-047	Level of anti-PD-1	Mean	SD	F-value	p-value	
Tumor Weight	WDR5-047 status	WDR5-047		0.2256	0.1051	75.88	<0.0001	
		Control		0.5988	0.2473			
	anti-PD-1 status			anti-PD-1	0.2788	0.1541	38.82	<0.0001
				Control	0.5456	0.2911		
	WDR5-047 Status x anti-PD-1 status	WDR5-047	WDR5-047	anti-PD-1	0.1488	0.0380	6.97	0.0134
				Control	0.3025	0.0935		
Control		anti-PD-1	0.4088	0.1040				
		Control	0.7888	0.1942				
Tumor Size	WDR5-047 Status	WDR5-047		213.4229	123.4092	58.32	<0.0001	
		Control		851.5887	506.8368			
	anti-PD-1 status			anti-PD-1	300.7270	194.1639	30.77	<0.0001
				Control	764.2846	580.5266		
	WDR5-047 Status x anti-PD-1 status	WDR5-047	WDR5-047	anti-PD-1	139.5968	31.4927	14.29	0.0008
				Control	287.2491	138.5125		
Control		anti-PD-1	461.8573	143.0007				
		Control	1241.3201	427.5947				

Table S7 Two-factor ANOVA results of WT (Scramble)/*Spp1* KO and anti-PD-1 immunotherapy on tumor weight and size.

Outcome	Effect in Model	Level of Cell Type	Level of anti-PD-1	Mean	SD	F-value	p-value
Tumor Weight	Cell type	Scramble		0.29	0.14	27.01	<0.0001
		<i>Spp1</i> KO		0.14	0.04		
	anti-PD-1 status		anti-PD-1	0.16	0.05	14.20	0.0011
			IgG	0.25	0.14		
	Cell type x anti-PD-1 status	Scramble	anti-PD-1	0.21	0.02	5.28	0.0319
			IgG	0.38	0.15		
<i>Spp1</i> KO		anti-PD-1	0.12	0.03			
		IgG	0.17	0.04			
Tumor Size	Cell type	Scramble		416.76	170.39	60.07	<0.0001
		<i>Spp1</i> KO		147.77	59.95		
	anti-PD-1 status		anti-PD-1	180.43	125.87	21.53	0.0001
			IgG	322.13	190.77		
	Cell type x anti-PD-1 status	Scramble	anti-PD-1	305.13	97.94	2.59	0.1227
			IgG	522.40	161.94		
<i>Spp1</i> KO		anti-PD-1	91.54	21.79			
		IgG	196.96	29.20			