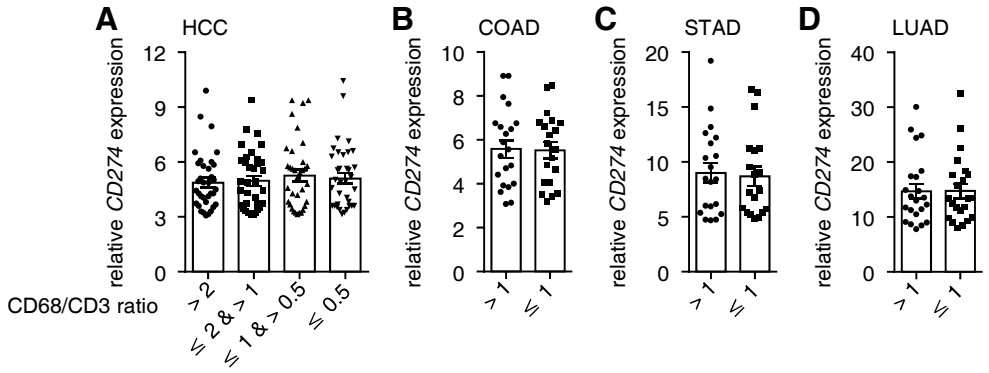
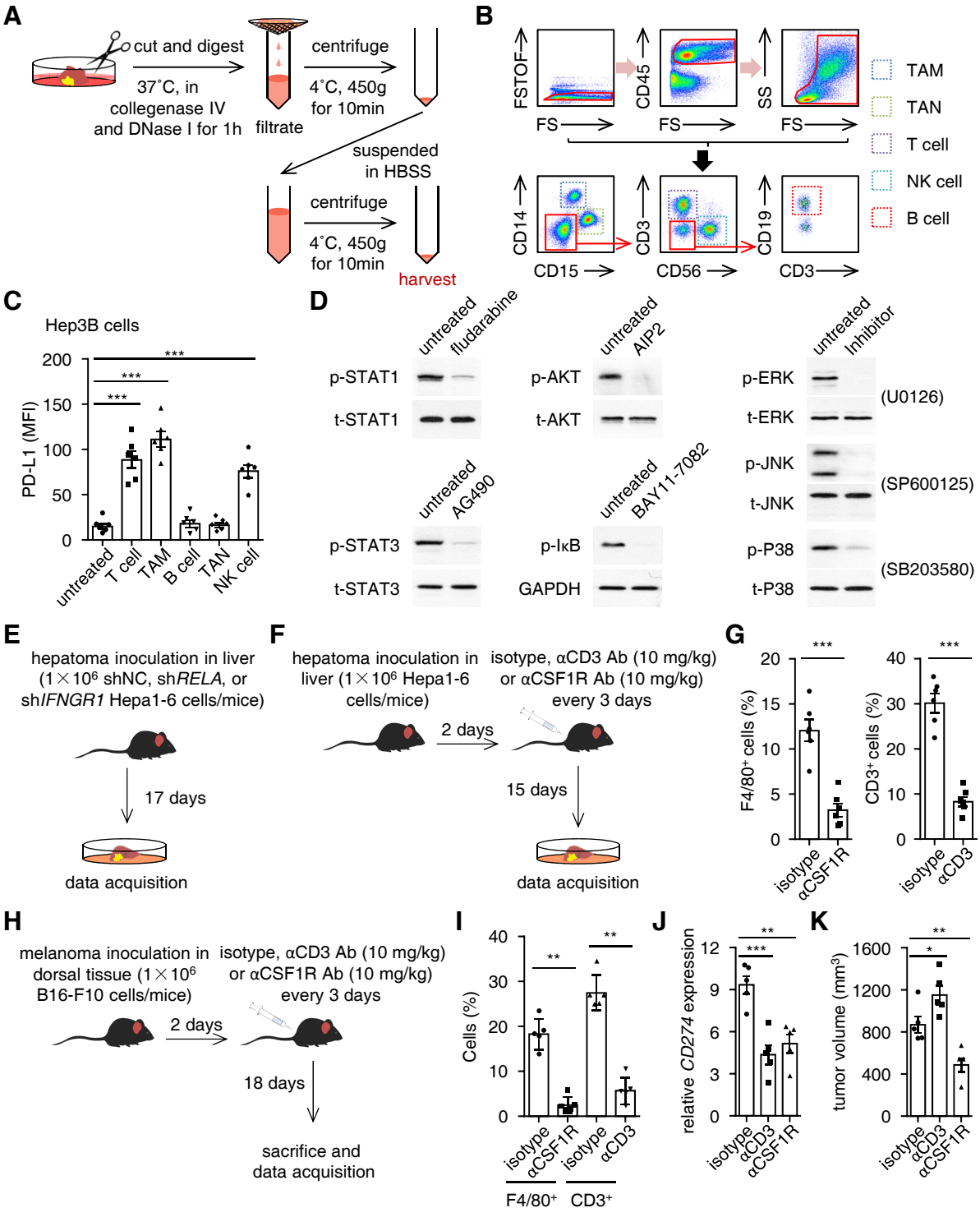
Supplementary information

Supplemental Figure 1



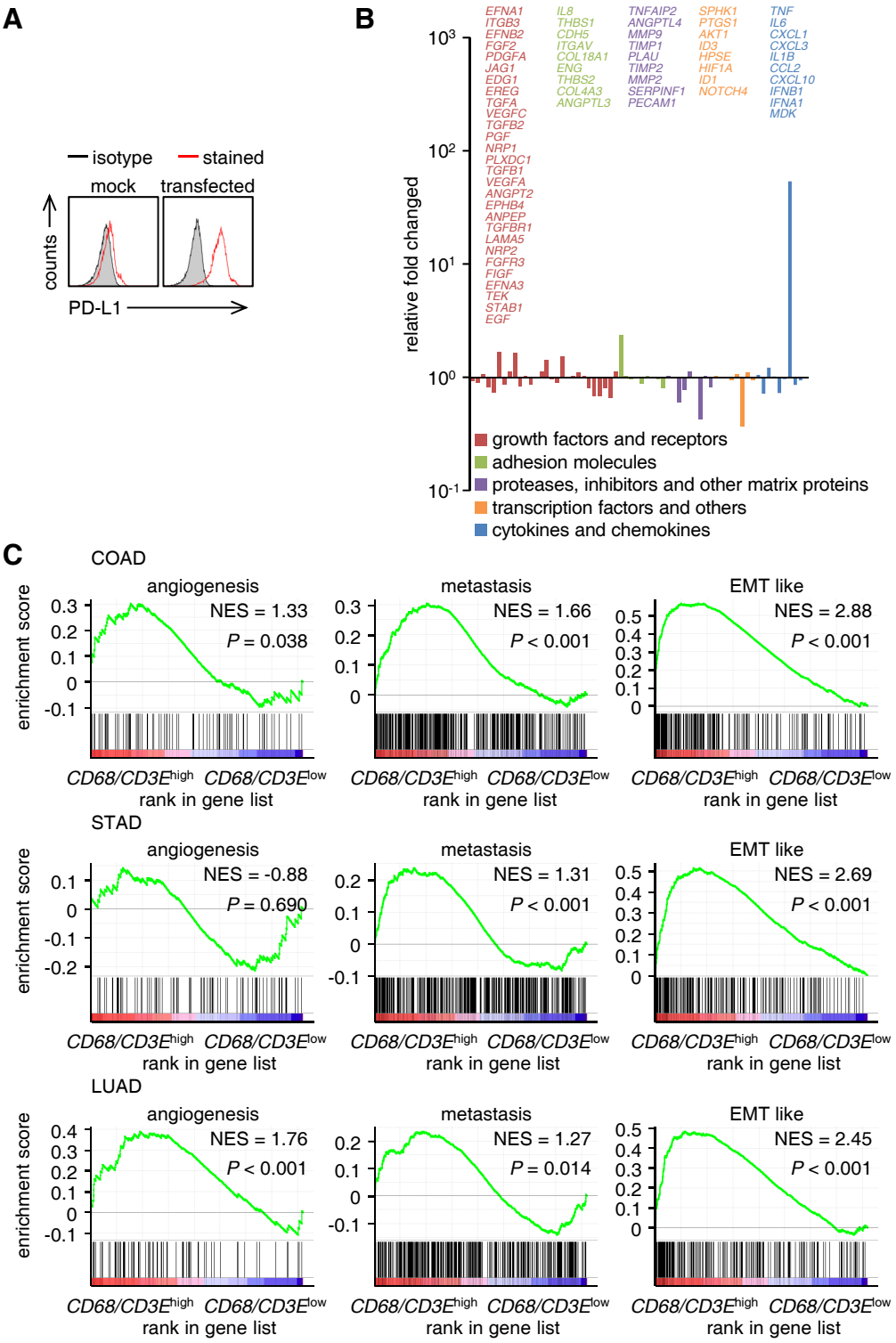
Supplemental Figure 1. Immune landscapes of PD-L1^{high} tumors determine patients' clinical outcomes. (**A**-**D**) *CD274* expression in tumor tissues with different patterns of CD3 and CD68 distribution. *CD274*^{high} patients were divided into four groups or two groups according to the ratio of macrophages to CD3^{+} T cells in tumor as described in Figure 2, **E** and **H**. Data represent mean ± SEM.

Supplemental Figure 2



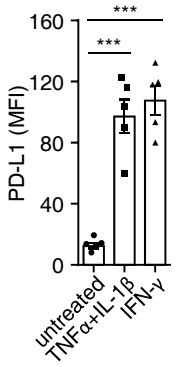
Supplemental Figure 2. Distinct induction patterns of cancer cell PD-L1 by TAM and T cells. (**A**) Procedure for preparing single-cell leukocyte suspensions from human HCC tissue. (**B**) Gating strategies for FACS analysis and sorting B cells, T cells, NK cells, neutrophils, and macrophages from HCC tissue. Representative plots of cells isolated from tumor tissue showed that mononuclear cells from samples were first gated for singlet (FS-TOF vs. FS) and then for leukocytes (FS vs. CD45 and FS vs. SS), and finally for the indicated marker of specific cell types (n = 6). (**C**) Hep3B cells were left untreated or were incubated with CM from indicated immune cells isolated from HCC tissues. Expression of PD-L1 were determined by FACS on day 3 (n = 6). (**D**) Inhibitory efficiencies of indicated inhibitors on the activation of STAT, MAPK, PI3K, and NF-κB signaling pathways in TIL-CM-treated HepG2 cells. (**E**) Wild type (shNC), P65 knockdown (sh*RELA*), or IFN-γ receptor knockdown (sh*IFNGR1*) Hepa1-6 cells were inoculated in livers of C57BL/6 mice for 17 days as indicated. (**F**-**K**) Mice bearing Hepa1-6 hepatoma (**F**) or B16-F10 melanoma (**H**) were injected with isotype, anti-CD3 Ab, or anti-CSF1R Ab every 3 day as indicated. Effects of anti-CSF1R and anti-CD3 Abs on the infiltration of macrophages and T cells, respectively, were determined in mouse tumor tissues (**G** and **I**, n = 6 for **G** and n = 5 for **I**). *CD274* expression in tumor tissues (**J**) and tumor volume (**K**) of melanoma were analyzed (n = 5). Data represent mean ± SEM. Results are representative of three separate experiments. $^{*}P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$, 1-way ANOVA with Dunett's post-test (**C**, **J**, and **K**) or Student's t test (**G** and **I**).

Supplemental Figure 3



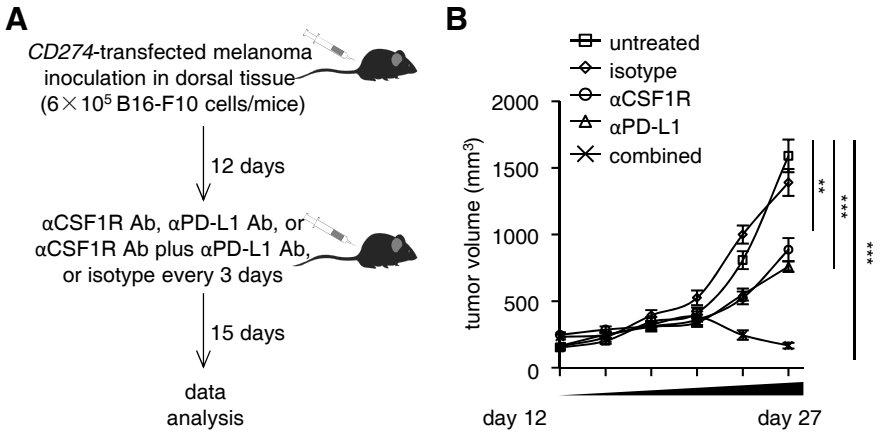
Supplemental Figure 3. Macrophages and T cells induce PD-L1⁺ cancer cells with distinct hallmarks. (**A**) FACS analysis of PD-L1 transduction rates in HepG2 cells (n = 3). (**B**) Fold changes of protumorigenic genes mRNA levels in T-cell-CM-generated PD-L1⁺ HepG2 cells compared with untreated HepG2 cells were analyzed by SuperArray Real-Time PCR. (**C**) Gene set enrichment analysis of angiogenesis signature, metastasis signature, and EMT like signature in *CD68/CD3E*^{high} samples versus *CD68/CD3E*^{low} counterparts within *CD274*^{high} COAD, STAD, and LUAD patients from TCGA data set.

Supplemental Figure 4



Supplemental Figure 4. TNFα/IL-1β and IFN-γ induce cancer cell PD-L1, respectively. HepG2 cells were left untreated or were incubated with TNFα plus IL-1β or IFN-γ. Expression of PD-L1 were determined by FACS on day 3 (n = 5). Data represent mean ± SEM. Results are representative of three separate experiments. ***P < 0.001, 1-way ANOVA with Dunett's post-test.

Supplemental Figure 5



Supplemental Figure 5. Depleting macrophage augments immunotherapeutic efficacy of a PD-L1 antibody in mice melanoma. (**A**) Mice bearing B16-F10 melanoma in dorsal tissues for 12 days were left untreated or were treated with isotype, αCSF1R Ab, αPD-L1 Ab, or αCSF1R Ab plus αPD-L1 Ab as described. (**B**) Tumor sizes over the indicated time were analyzed (n = 5). Data represent mean ± SEM. $^{**}P < 0.01$ and $^{***}P < 0.001$, 1-way ANOVA with Bonferroni's post-test (**B**).

Supplemental Table 1. Clinical characteristics of the 382 HCC patients

Patient characteristics	Cohort 1	Cohort 2
No. of patients	345	37
Age, years (median, range)	49, 17–75	53, 19–78
Gender (male/female)	308/37	31/6
HbsAg (negative/positive)	42/303	3/34
Cirrhosis (absent/present)	68/277	15/22
ALT, U/L (median, range)	44, 9–1590	32.3, 16–108.2
AFP, ng/ml (≤ 25/> 25)	101/244	14/23
Tumor size, cm (≤ 5/> 5)	122/223	17/20
Tumor multiplicity (solitary/multiple)	271/74	27/10
Vascular invasion (absent/present)	311/34	29/8
Intrahepatic metastasis (no/yes)	283/62	37/0
TNM stage (I+II/III+IV)	241/104	27/10
Tumor differentiation (I+II/III+IV)	270/75	18/19
Fibrous capsule (absent/present)	71/274	16/21

Abbreviations: HbsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AFP, α-fetoprotein; TNM, tumor node metastasis.

Note: Patients in hepatocellular carcinoma cohort 1 contributed to the paraffin-embedded samples for IHC staining and real time-PCR that were used in analyses of PD-L1 expression, cell distribution, correlation, and patient prognosis; patients in hepatocellular carcinoma cohort 2 contributed fresh samples.

Supplemental Table 2. Information of tumor samples from TCGA data set

Tumor	Abbreviation	Cohort	Number
Adrenocortical carcinoma	ACC	Provisional	79
Bladder Urothelial Carcinoma	BLCA	Provisional	408
Breast invasive carcinoma	BRCA	Provisional	817
Cervical squamous cell carcinoma and endocervical adenocarcinoma	CESC	Provisional	306
Cholangiocarcinoma	CHOL	Provisional	36
Colon adenocarcinoma	COAD	Provisional	382
Lymphoid Neoplasm Diffuse Large B cell Lymphoma	DLBC	Provisional	48
Esophageal carcinoma	ESCA	Provisional	185
Glioblastoma multiforme	GBM	Provisional	154
Head and Neck squamous cell carcinoma	HNSC	Provisional	522
Kidney Chromophobe	KICH	Provisional	66
Kidney renal clear cell carcinoma	KIRC	Provisional	534
Kidney renal papillary cell carcinoma	KIRP	Provisional	291
Acute Myeloid Leukemia	LAML	Provisional	172
Brain Lower Grade Glioma	LGG	Provisional	530
Liver hepatocellular carcinoma	HCC	Provisional	373
Lung adenocarcinoma	LUAD	Provisional	230
Lung squamous cell carcinoma	LUSC	Provisional	501
Mesothelioma	MESO	Provisional	87
Ovarian serous cystadenocarcinoma	OV	Provisional	307
Pancreatic adenocarcinoma	PAAD	Provisional	179
Pheochromocytoma and Paraganglioma	PCPG	Provisional	184
Prostate adenocarcinoma	PRAD	Provisional	498
Sarcoma	SARC	Provisional	263
Skin Cutaneous Melanoma	SKCM	Provisional	472
Stomach adenocarcinoma	STAD	Provisional	415
Testicular Germ Cell Tumors	TGCT	Provisional	156
Thyroid carcinoma	THCA	Provisional	509
Thymoma	THYM	Provisional	120
Uterine Corpus Endometrial Carcinoma	UCEC	Provisional	177
Uterine Carcinosarcoma	UCS	Provisional	57
Uveal Melanoma	UVM	Provisional	80

Supplemental Table 3. Genes used in GSEA analysis

Tumor necrosis factor signature									
ORM1	*TLR3*	*TRIM27*	*LGALS9*	*WNT5A*	*H0Y858*	*IL12B*	*TICAM1*	*IFIH1*	*THBS1*
NOD2	*CD34*	*LEP*	*RIPK1*	*ISL1*	*NLRC3*	*UBE2J1*	*CYBA*	*SLAMF1*	*ZBTB20*
HMGB1	*PF4*	*LTF*	*GAS6*	*GPR18*	*CLEC4A*	*APP*	*FCER1G*	*CHRNA7*	*TNFRSF8*
HSF1	*FOXP3*	*CD14*	*TLR4*	*HLA-E*	*PTAFR*	*TBC1D23*	*ACP5*	*TIRAP*	*ARFGEF2*
CCL19	*CACTIN*	*GHSR*	*ADIPOQ*	*TNFAIP3*	*LRRK2*	*HDAC2*	*CYBB*	*HAVCR2*	*ARHGEF2*
LY96	*IRAK3*	*TWIST1*	*ZFP36*	*TLR1*	*ANGPT1*	*CCR2*	*HSPB1*	*SPN*	*TNFRSF11A*
CD2	*POMC*	*MAVS*	*LBP*	*ARG2*	*CD36*	*DHX9*	*RARA*	*PTPN22*	*TNFRSF21*
AXL	*NFKBIL1*	*FOXP1*	*RASGRP1*	*CCL3*	*ZC3H12A*	*GHRL*	*AZU1*	*PYCARD*	*TNFRSF10D*
MC1R	*AKAP8*	*GPNMB*	*BPI*	*DDX58*	*CARD9*	*NFATC4*	*LILRA4*	*RIPK2*	*MAPKAPK2*
DEFB114	*C5AR2*	*ERRFI1*	*LILRB1*	*SELENOK*	*PIK3R1*	*IL10*	*CLU*	*BCL3*	*ORM2*
SYT11	*DDT*	*NOD1*	*ARRB2*	*TXNDC17*	*SASH3*	*IL23A*	*AZI2*	*TRAIP*	*OCSTAMP*
HAMP	*COL1A1*	*CLDN18*	*TRAF3*	*CD40LG*	*TNFSF9*	*TCL1A*	*PLVAP*	*ILK*	*TNFRSF1A*
CCL16	*CCL25*	*TRAF1*	*APOB*	*SPPL2A*	*SPPL2B*	*ZNF675*	*POSTN*	*KARS*	*ADAMTS13*
CCL24	*PYDC2*	*CASP1*	*ENDOG*	*TNFRSF6B*	*TNFSF8*	*CD70*	*ICAM1*	*ST18*	*TNFRSF13C*
PRKN	*SNRNP70*	*CX3CL1*	*SLC2A4*	*RBCK1*	*HMHB1*	*VCAM1*	*GSDME*	*MAP4K3*	*EDA2R*
CHI3L1	*IGBP1*	*CARD14*	*SPHK1*	*GPS2*	*PIAS4*	*PID1*	*NGFR*	*TANK*	*TNFRSF10A*
CCL17	*KRT8*	*TNFRSF9*	*CCL7*	*CCL8*	*COMMD7*	*GATA3*	*TAX1BP1*	*WDR35*	*TNFRSF17*
TDGF1	*FABP4*	*PCK1*	*HYAL2*	*IKBKB*	*CCDC3*	*RELT*	*AIM2*	*HYAL1*	*TNFRSF13B*
SFRP1	*PRPF8*	*EDAR*	*PTK2B*	*RPS6KB1*	*RPS3*	*EDA*	*RORA*	*ZFP36L1*	*TNFRSF25*
CARD8	*F2RL1*	*UBD*	*MYOG*	*MYOD1*	*CD27*	*TNFSF4*	*CCL4*	*KAT2A*	*PPARGC1A*
TNFSF11	*AKT1*	*PTGS2*	*NFKB1*	*GBA*	*MAP2K7*	*ACOD1*	*INPP5K*	*ABCC2*	*TNFRSF10C*
CCL21	*HIPK1*	*CCL3L1*	*CPNE1*	*CIB1*	*ZFAND6*	*YBX3*	*SELE*	*CCL22*	*TNFRSF19*
RFFL	*GPER1*	*HAS2*	*TNFRSF4*	*HIST1H2BJ*	*AFF3*	*MAPK1*	*CALCA*	*CCL13*	*TNFRSF11B*
CCL11	*CCL5*	*IKBKG*	*PYDC1*	*LTBR*	*NPNT*	*RACK1*	*SYK*	*CD40*	*TNFRSF10B*
MADD	*FAS*	*XCL1*	*EDARADD*	*BRCA1*	*TRADD*	*NKX3-1*	*LTA*	*TNF*	*ANKRD1*
LIMS1	*PELI3*	*BIRC2*	*BIRC3*	*CDIP1*	*ADAM9*	*MAP3K5*	*GPD1*	*TRPV1*	*MAP3K14*
SMPD4	*NOL3*	*ERBIN*	*CCL20*	*ADAM17*	*GCH1*	*FZD5*	*CASP8*	*HSPA1B*	*NLRP2B*
PIAS3	*GBP3*	*XCL2*	*EDN1*	*CARD16*	*TMSB4X*	*RELA*	*NFKBIA*	*CXCL8*	*TNFRSF14*
BAG4	*KCNJ11*	*TNFSF13B*	*KLF2*	*TNFSF15*	*CCL18*	*CCL23*	*ADAM10*	*HDAC4*	*ADAMTS12*
CCL2	*CASP3*	*CLIP3*	*CLDN1*	*TNFRSF18*	*NFE2L2*	*GBP2*	*SIRT1*	*NUB1*	*HSPA1A*
CASP4	*TNFSF13*	*PTPN2*	*CCL26*	*DAB2IP*	*FOXO3*	*MAPK14*	*KRT18*	*IL18BP*	*CCL4L1*

TNFSF14	*TNFSF12*	*MAPK3*	*RNF31*	*STAT1*	*CXCL16*	*CCL14*	*OCLN*	*CCL1*	*ADAMTS7*
GBP1	*SHARPIN*	*ZFP36L2*	*TNFSF18*	*CYLD*	*LTB*	*ASS1*	*CRHBP*	*PCK2*	*TNFRSF1B*
CHUK	*TRIM32*	*APOA1*	*TRAF2*	*CEBPA*	*TSPO*	*OTULIN*	*CCL15*	*TLR2*	*TNFRSF12A*
YTHDC2	*CD58*	*DCSTAMP*	*HYAL3*						
Interleukin-1 signature									
AES	*IRAK4*	*MAPK13*	*KMO*	*UBE2V1*	*CCL16*	*CCL25*	*ZNF675*	*TOLLIP*	*S100A13*
MAP3K8	*LGALS9*	*UBB*	*CCL24*	*ICAM1*	*ST18*	*CUL1*	*CX3CL1*	*NOD2*	*ADAMTS12*
IL1RL2	*CHI3L1*	*SQSTM1*	*IGBP1*	*OTUD4*	*TANK*	*PELI3*	*CCL17*	*CCL7*	*RPS6KA4*
CYBA	*PCK1*	*HYAL2*	*IKBKB*	*TRIM63*	*HYAL1*	*PLCB1*	*CD38*	*TAB3*	*MAP3K3*
IL1RN	*EPO*	*IL1B*	*IL1A*	*SFRP1*	*YY1*	*CCL4*	*IL1R1*	*RORA*	*NFKB1*
ANXA1	*ACOD1*	*ABCC2*	*CCL3L1*	*MYD88*	*PRKCI*	*SELE*	*SOX9*	*CCL22*	*SLC30A8*
CACTIN	*HAS2*	*TRAF6*	*GCLC*	*CCL13*	*CCL11*	*AZU1*	*IRAK1*	*VRK2*	*CITED1*
IKBKG	*UPF1*	*SKP1*	*RPS27A*	*MAPK11*	*TAB1*	*RC3H1*	*XCL1*	*NLRP7*	*TNFRSF11A*
IRAK3	*CCL8*	*NKX3-1*	*ANKRD1*	*HIF1A*	*EGR1*	*CCL21*	*UBE2N*	*CCL20*	*RPS6KA5*
OTUB1	*IRAK2*	*GBP3*	*TAB2*	*XCL2*	*EDN1*	*RELA*	*NFKBIA*	*CCL3*	*ADAMTS7*
USP10	*CD40*	*ETS1*	*BTRC*	*IL6*	*CXCL8*	*CCL18*	*CCL23*	*HDAC4*	*ZC3H12A*
CCL2	*UBA52*	*PRKCA*	*RBX1*	*GBP2*	*TNIP2*	*RIPK2*	*CCL26*	*DAB2IP*	*CEACAM1*
IL17A	*CCL5*	*PELI1*	*SNCA*	*CCL4L1*	*TFPI*	*UBC*	*MAPK3*	*IL1R2*	*PYCARD*
MTHFR	*PTGIS*	*TAF9*	*CCL14*	*CCL1*	*CEBPB*	*GBP1*	*RBMX*	*MYLK3*	*HYAL3*
SRC	*FGG*	*FGB*	*CCL19*	*NOD1*	*CCL15*	*KLF2*	*YTHDC2*	*FBXW11*	*CASP1*
IL1RAP	*JAK2*	*GSTP1*	*NLRP3*	*NLRP2*	*PANX1*	*ORM1*	*WNT5A*	*PYDC2*	*CHRNA7*
PML	*ISL1*	*SPHK1*	*CMA1*	*HMGB1*	*AIM2*	*NLRC4*	*SUCNR1*	*NLRP1*	*P2RX7*
INAVA	*CARD8*	*F2RL1*	*TLR4*	*F2R*	*ACP5*	*S1PR3*	*CPTP*	*GHSR*	*NLRP2B*
TNFAIP3	*TLR8*	*PYDC1*	*HSPB1*	*MEFV*	*FZD5*	*ARG2*	*CD36*	*GBP5*	*MAP3K7*
NLRP12	*CARD18*	*TRIM16*	*SMAD3*	*CARD16*	*FOXP1*	*ABCA1*	*GHRL*	*MR1*	*NLRP10*
CARD17	*ERRFI1*	*TLR6*	*CCR7*	*IFI16*	*ORM2*	*APOA1*	*GSDMD*	*ARRB2*	*GAS6*
IGHD	*PELI2*	*SAA1*	*NR1H4*	*CHUK*	*HDAC2*	*HAVCR2*	*IL10*		
Angiogenesis									
ABL1	*ACVRL1*	*ADAMTS9*	*ADGRA2*	*AGTR1*	*AKT3*	*ANGPT1*	*ANXA1*	*APELA*	*APLNR*
BMP4	*BMPER*	*CARD10*	*CCBE1*	*CDC42*	*CDH13*	*CIB1*	*CLEC14A*	*CREB3L1*	*DLL1*
DLL4	*E2F2*	*E2F7*	*E2F8*	*EFNB2*	*EGR3*	*ENG*	*EPHA2*	*EPHB4*	*EPN1*
EPN2	*ESM1*	*FGF1*	*FGF2*	*FGFBP1*	*FLT4*	*FOXC2*	*GATA2*	*GHRL*	*GHSR*
GPLD1	*GREM1*	*HDAC5*	*HDAC7*	*HDAC9*	*HMOX1*	*IL10*	*ITGA5*	*ITGB1*	*ITGB1BP1*

JAK1	*JCAD*	*JMJD6*	*KDR*	*KLF2*	*KLF4*	*LEF1*	*LOXL2*	*MAP2K5*	*MAP3K3*
MEOX2	*MMRN2*	*NGFR*	*NOTCH1*	*NR2E1*	*NR4A1*	*NRARP*	*NRP1*	*OTULIN*	*PARVA*
PDCD10	*PDPK1*	*PGF*	*PIK3C2A*	*PLK2*	*PPP1R16B*	*PTGS2*	*PTK2B*	*RAMP2*	*RHOA*
RHOJ	*RNF213*	*ROBO1*	*RSPO3*	*S100A1*	*SEMA3E*	*SEMA5A*	*SEMA6A*	*SLIT2*	*SMAD1*
SPRED1	*SRF*	*SRPX2*	*STARD13*	*SYNJ2BP*	*TBXA2R*	*TDGF1*	*TEK*	*THBS1*	*VEGFA*
VEGFB	*VEGFC*	*VEGFD*							
Metastasis									
ACTN4	*ADAM33*	*ADAMTS5*	*ADSL*	*AEBP1*	*AGRN*	*AGTRAP*	*AKR1B10*	*ALPK3*	*AMMECR1*
ANKRD10	*ANKRD52*	*ANXA2*	*AP1S2*	*ARFGAP1*	*ARG2*	*ARHGEF2*	*ARNTL2*	*ASAP1*	*ASNS*
ASPH	*ASRGL1*	*ATAD2*	*ATIC*	*B3GALNT1*	*B3GAT3*	*B3GNT5*	*BAMBI*	*BARD1*	*BCAS4*
BCAT1	*BCL11A*	*BOP1*	*BRD9*	*BUB1B*	*C11orf49*	*C12orf49*	*C18orf54*	*C19orf2*	*C1orf144*
C3orf14	*C4orf48*	*C8orf59*	*C9orf30*	*C9orf86*	*CA12*	*CABYR*	*CAPG*	*CBFA2T2*	*CBX2*
CBX5	*CBX6*	*CCDC165*	*CCDC64*	*CCDC93*	*CCDC97*	*CD109*	*CD24*	*CDC7*	*CDCA7*
CDCA7L	*CDK13*	*CDKN1C*	*CENPM*	*CHD7*	*CHFR*	*CHML*	*CHTF18*	*CIB2*	*CKAP4*
CLN6	*CLTB*	*COL1A2*	*COLEC12*	*COX5B*	*CPSF1*	*CREB3L1*	*CSNK1E*	*CTHRC1*	*CTNND2*
DDHD1	*DDIT4*	*DDOST*	*DDX25*	*DEAF1*	*DEF6*	*DENND1A*	*DENR*	*DGKZ*	*DHRS13*
DKK1	*DLG5*	*DLGAP4*	*DMKN*	*DNAJA4*	*DNAJC10*	*DPP3*	*DTNA*	*DTNBP1*	*DTYMK*
DUSP22	*DUSP9*	*E2F1*	*ECT2*	*EHD2*	*ENAH*	*ENO2*	*EZH2*	*FABP5*	*FAM110A*
FAM129B	*FAM171B*	*FAM50A*	*FAM58A*	*FARP1*	*FBLIM1*	*FBLN1*	*FBXO41*	*FBXW12*	*FERMT1*
FLCN	*FLJ33996*	*FLJ43489*	*FLNA*	*FNDC3B*	*FOXM1*	*FOXO6*	*FOXQ1*	*G6PD*	*GAPDHP62*
GAS2L3	*GAS5*	*GBP2*	*GCNT3*	*GDI1*	*GLDN*	*GNB2L1*	*GNG4*	*GNPDA1*	*GORAB*
GPR107	*GPR172A*	*GPRC5B*	*GPX8*	*GTPBP1*	*GTSE1*	*GXYLT2*	*GYG1*	*HDAC1*	*HEATR7A*
HES4	*HIC2*	*HKDC1*	*HLA-DQA1*	*HMGA1*	*HMGB3*	*HOXA5*	*HOXD8*	*HPS1*	*HRAS*
HYOU1	*IFRD1*	*IGF2BP2*	*IGF2BP3*	*IGSF3*	*IKZF4*	*INTS8*	*IPPK*	*ITPR3*	*JMY*
JRK	*KCNH2*	*KCNQ1*	*KCTD2*	*KIAA0090*	*KIAA0101*	*KIAA1244*	*KIAA1522*	*KIAA1919*	*KIF18B*
KIF2A	*KIFC2*	*KLHL29*	*KRT23*	*LASP1*	*LIMK2*	*LLGL1*	*LOC100216479*	*LOC100288911*	*LOC100506935*
LOC100507392	*LOC155060*	*LOC286437*	*LOC440416*	*LOC727820*	*LOC92659*	*LRP11*	*LRPPRC*	*LRRC16A*	*LUZP1*
MALAT1	*MAP1B*	*MAP2*	*MAP3K4*	*MAP4*	*MAP4K4*	*MAP7D2*	*MAPK13*	*MBNL1*	*MCAM*
MCOLN3	*MEAF6*	*MECOM*	*MEP1A*	*MFSD10*	*MICALL1*	*MMD*	*MMP11*	*MMP12*	*MORC2*
MPHOSPH9	*MRS2*	*MRTO4*	*MTHFD1L*	*MXD1*	*MYBL2*	*MYEF2*	*MYLIP*	*N4BP2L2*	*NACA*
NAV3	*NDE1*	*NEIL3*	*NETO2*	*NFKBIB*	*NLN*	*NOL3*	*NPAS2*	*NPNT*	*NQO1*
NSMAF	*NUB1*	*NUDT14*	*NUF2*	*NUMBL*	*NUP43*	*NUPR1*	*OLA1*	*PACSIN2*	*PAFAH1B3*
PAM	*PAQR5*	*PCNXL3*	*PCSK5*	*PDCD2*	*PDE4C*	*PDK1*	*PDZK1IP1*	*PES1*	*PFKFB4*

PGF	*PHF19*	*PHF21A*	*PHPT1*	*PKIB*	*PKM2*	*PKP4*	*PLAG1*	*PLAGL1*	*PLBD2*
PLCB1	*PLD1*	*PLXNA1*	*PLXNC1*	*PNKP*	*POMZP3*	*POPDC3*	*POU2AF1*	*PPIL2*	*PPM1F*
PRPF31	*PRR11*	*PRRC2A*	*PRRC2B*	*PSMC3IP*	*PTGES*	*PTGFRN*	*PTGR1*	*PTPN14*	*PTPRM*
PURB	*PUSL1*	*PWWP2B*	*PYCRL*	*RAB3GAP2*	*RAD54B*	*RAVER1*	*RBBP4*	*RBM10*	*RCAN3*
RCC2	*REXO4*	*RHOBTB1*	*RNF145*	*RRAS*	*RRP12*	*RRP7A*	*RUVBL2*	*SAC3D1*	*SBNO1*
SCAMP5	*SCRIB*	*SEMA3F*	*SEP9*	*SERINC2*	*SERPINB1*	*SERPINE2*	*SERPINH1*	*SESTD1*	*SF3A2*
SHC1	*SHKBP1*	*SLC16A7*	*SLC22A15*	*SLC25A19*	*SLC25A24*	*SLC25A29*	*SLC25A36*	*SLC2A6*	*SLC36A1*
SLC39A10	*SLC39A4*	*SLC44A3*	*SLC45A4*	*SLC6A8*	*SLC7A11*	*SMG5*	*SMOX*	*SMPD2*	*SNAP25*
SNAPC4	*SNRNP48*	*SNRPA*	*SNRPN*	*SOHLH2*	*SORT1*	*SOX4*	*SOX9*	*SPAG4*	*SPINK1*
SPINT1	*SPON2*	*SSBP4*	*ST14*	*STK39*	*STOX2*	*STRBP*	*SULT1C2*	*SURF2*	*SUSD4*
TAF3	*TAX1BP3*	*TBC1D13*	*TCF3*	*TCIRG1*	*TDG*	*TEAD2*	*TECPR1*	*TGFB2*	*THEM4*
TKT	*TMCC1*	*TMCO4*	*TMED9*	*TMEM165*	*TMEM194A*	*TMEM237*	*TMF1*	*TMSB10*	*TNIP2*
TNPO1	*TOB2*	*TOX3*	*TPD52L2*	*TRAF5*	*TRAPPC4*	*TRIP10*	*TRIP13*	*TRPC1*	*TRPS1*
TSHZ2	*TSSC4*	*TTLL7*	*TUBB2A*	*TUFT1*	*TWIST1*	*UBAP2*	*UBAP2L*	*UBE2O*	*UBE2Q2*
UPF3B	*URB2*	*USP34*	*USP42*	*USP48*	*VANGL1*	*VCAN*	*VGLL4*	*VSIG10L*	*WDFY2*
WDR5	*WDR54*	*WFIKKN1*	*WHSC1*	*YARS*	*ZC3H3*	*ZCCHC7*	*ZDHHC24*	*ZFP41*	*ZIC2*
ZMYM3	*ZMYND19*	*ZNF234*	*ZNF239*	*ZNF432*	*ZNF532*	*ZNF618*	*ZNF704*	*ZNF721*	*ZNF765*
ZNF777	*ZNF789*	*ARHGEF1*	*ATXN2L*	*BIRC5*	*C20orf194*	*CARD8*	*CCNE1*	*CHD2*	*RAPGEF1*
COL1A1	*EFCAB2*	*GNAS*	*ITGA2*	*MAGEA1*	*NEAT1*	*PIGT*	*RRAGD*	*DBN1*	*FAM199X*
GRK6	*KIAA0513*	*MARS*	*NRP1*	*PLP2*	*SEMA3C*	*DGCR2*	*FIGN*	*HJURP*	*LAMB1*
MKNK1	*OTUD3*	*PPP2R4*	*SH2B1*	*DNM1L*	*FXYD3*	*HUNK*	*LOC286052*	*MTMR2*	*PDIA4*
PTP4A3	*SLC2A1*	*TMEM201*	*TRABD*	*TTLL4*	*UCP2*	*VSIG10*	*ZCCHC17*	*ZNF302*	*ALDOA*
ALDH18A1	*CAPN10*	*DGCR14*	*FUS*	*IRAK1*	*MAPK3*	*ORAI2*	*PTMA*	*ARHGAP4*	*CCL28*
DNAJC6	*GLS*	*KIAA0485*	*MIR210HG*	*PDGFA*	*RAD54L*	*ATP13A2*	*CEP164*	*EEF1A2*	*GRAMD1A*
LAMA5	*MTHFD2*	*PIDD*	*ROBO1*	*BCORL1*	*COL11A2*	*FAM178A*	*HIF1AN*	*LOC283508*	*NDOR1*
PLEKHG2	*SELM*	*C1orf93*	*CTSC*	*FHOD3*	*HSPBAP1*	*MACROD2*	*NRCAM*	*PPP1R9A*	*SGSH*
SLC29A4	*SLFN13*	*SOAT1*	*SPTBN1*	*SYNCRIP*	*TFAP2C*	*TMEM200B*	*TPM2*	*TSTA3*	*UCHL1*
VPS13C	*ZC3HAV1*	*ZNF292*	*ZNF827*	*SMARCE1*	*SOCS7*	*SSBP2*	*TACC3*	*TFPT*	
EMT like									
TGFBI	*IGFBP3*	*MMP1*	*ITGB1*	*LAMC2*	*PDPN*	*TNC*	*LAMB3*	*VIM*	*CA9*
LAMA3	*ITGA6*	*COL17A1*	*CD99*	*PTHLH*	*GJA1*	*LTBP1*	*ITGB6*	*LIMA1*	*DNAJC3*
ITGA5	*ODC1*	*SERPINE2*	*AREG*	*BNIP3*	*MMP3*	*P4HA1*	*SLC2A1*	*FHL2*	*EDN1*
SDC1	*PRSS23*	*NPNT*	*RAMP1*	*CDH13*	*DST*	*MMP2*	*ITGB4*	*PTK7*	*CTSA*

AKR1C1	*DLK2*	*PXN*	*LEPREL1*	*PSMD2*	*PFN2*	*CSRP2*	*SLC16A1*	*PFKP*	*CNN3*
MMP10	*INHBA*	*KRT6B*	*MMP9*	*G0S2*	*CDH1*	*SPRR1B*	*ECM1*	*CD68*	*C14orf1*
HTRA1	*SQRDL*	*P4HA2*	*F3*	*TMEM154*	*CYB5R1*	*LOC100862671*	*IL1RN*	*FEZ1*	*SLC39A1*
KYNU	*GJB5*	*DHCR7*	*MBOAT2*	*MEG3*	*EMP3*	*DSC2*	*SDC4*	*UAP1*	*EFEMP1*
DHRS7	*OPTN*	*COL4A2*	*ANXA3*	*AHNAK2*	*ANXA8*	*HERPUD1*	*CD40*	*SERINC1*	*DFNA5*
FN1	*CLU*	*COL1A1*	*TAGLN*	*AXL*	*KRT8*	*CTHRC1*	*TMEM45A*	*LEPRE1*	*RAP1B*
MUL1	*FRMD6*	*MAGED1*	*CTSL1*	*GADD45B*	*CTGF*	*KDELR3*	*CDH11*	*SLC31A2*	*TGM2*
COL5A2	*CXCL13*	*AMTN*	*TCF25*	*IL32*	*LINC00152*	*GLIPR1*	*TMEM40*	*HIST1H2BG*	*PDLIM7*
SPATA20	*IGFL2*	*GALNT2*	*RALA*	*FSTL1*	*NIPSNAP1*	*SEMA3C*	*CDKN1A*	*DSG2*	*PRSS8*
MFSD1	*LGALS1*	*NNMT*	*SERPING1*	*IGFBP7*	*C1S*	*CD74*	*SERPINF1*	*SPARC*	*RAB8A*
IFITM2	*C1R*	*S100A4*	*ANGPTL4*	*GPX3*	*GSTA1*	*SAT1*	*SPP1*	*CCL2*	*MAPRE1*
S100A16	*MT2A*	*TIMP3*	*TPPP3*	*MYADM*	*PLIN2*	*SPARCL1*	*LSP1*	*TSPAN4*	*ERGIC2*
SMIM3	*SERPINA3*	*CYR61*	*ADAMTS1*	*SELM*	*MLKL*	*NDUFAF3*	*LUM*	*NMRK1*	*GLB1*
TIMP1	*TMEM179B*	*CXCL14*	*DKK3*	*SERPINH1*	*PRKCDBP*	*BGN*	*SLC7A8*	*SLC38A5*	*TSR2*
KLK5	*THBS2*	*CAV1*	*CXCR7*	*ADM*	*ANXA5*	*FSTL3*	*PLEK2*	*TNFRSF12A*	*IL1R2*
IGFBP6	*SLC3A2*	*SERINC2*	*PDLIM1*	*CD24*	*IVNS1ABP*	*FTH1*	*NDUFA4L2*	*MFAP2*	*SLC20A1*
GJB2	*APP*	*LOX*	*MT1X*	*SLC16A3*	*WFDC2*	*TNFRSF6B*	*SULF2*	*FCGRT*	*RNF25*
PLD3	*DNPH1*	*MMP28*	*TCIRG1*	*CTSH*	*MMP13*	*IGFL1*	*CCDC115*	*GAMT*	*BPGM*
PLEKHA1	*SGK1*	*CRABP2*	*ANXA4*	*TPST1*	*GLTSCR2*	*KRT14*	*SDC2*	*TMEM14C*	*GJB6*
PIK3IP1	*TLR2*	*TNFSF10*	*PLAU*	*GSN*	*WDR91*	*ALDH2*	*EXT2*	*SPHK1*	*IFI30*
NINJ1	*SLC39A14*	*FTSJ1*	*ATP1B1*	*COL7A1*	*BMP1*	*RTKN*	*PTK2*	*CTNNAL1*	*PLS3*
ECH1	*BECN1*	*THBS1*	*PSMD13*	*SMARCA1*	*PDCL3*	*LEMD1*	*ACTR3*	*VAMP3*	*SOD2*
HSPA5	*GALNT3*	*SERPINB5*	*DDX47*	*NANS*	*TVP23B*	*ADAM9*	*TM9SF2*	*PAFAH1B2*	*TPM1*
EFNA5	*KLF7*	*TP63*	*SF3A3*	*CCL20*	*CMTM6*	*WDR18*	*USP10*	*CLIC4*	*TOR1A*
GMPPA	*RPL21P28*	*SERPINE1*	*TRIM16*	*RBP1*	*NDRG1*				

Supplemental Table 4. Clinical characteristics of the 249 cancer patients

Stomach Adenocarcinoma Patient Characteristics	Cases
Number of patients	78
Age (yr; median, range)	54, 21–74
Gender (male/female)	51 / 27
Tumor depth (pT2/pT3)	15 / 63
Lymph node metastasis (pN0/pN1+pN2+pN3)	41 / 37
Histologic classification (intestinal/diffuse/mixed)	45 / 28 / 5
Tumor size (cm; ≤4/>4)	35 / 43
Tumor location (higher/middle/lower/others)	40 / 16 / 17 / 5
Borrmann type (I+II/III+IV)	30 / 48
Colon Adenocarcinoma Patient Characteristics	Cases
Number of patients	82
Age (yr; median, range)	52, 31-82
Gender (male/female)	41 / 41
Tumor stage (pT2/pT3)	21 / 61
Lymphatic invasion (yes/no)	12 / 70
Differentiation (well/moderate/poor)	60 / 17 / 5
Vascular emboli (yes/no)	12 / 70
Tumor location (right side/left side)	57 / 25
Lung Adenocarcinoma Patient Characteristics	Cases
No. of patients	89
Age, years (median, range)	67, 42–85
Gender (male/female)	49 / 40
Tumor stage (I+II/III+IV)	60 / 29
Tumor size (cm; ≤3/>3)	72/17
lymphovascular invasion (yes/no)	6/83
pleural invasion (yes/no)	20/69
Tumor differentiation (well/moderate/poor)	20/46/23
Tumor location (Left/Right/Overlapping)	35/53/1
smoking habbit (yes/no)	59/30

Supplemental Table 5. Blocking effects of indicated cytokines in co-culture system by mAbs

Treatment	**TNF-α** (pg/ml)	**IL-1β** (pg/ml)	**IL-6** (pg/ml)	**IL-12** (pg/ml)	**TGF-β** (pg/ml)	**IFN-γ** (pg/ml)
Untreated	2317 ± 212	487 ± 38	7254 ± 841	123 ± 21	1638 ± 224	1263 ± 146
Isotype	2128 ± 128	526 ± 28	6834 ± 523	142 ± 12	1873 ± 156	1337 ± 96
αTNF-α	56 ± 4	453 ± 21	7072 ± 611	121 ± 33	1453 ± 278	1289 ± 226
αIL-1β	2008 ± 138	38 ± 6	6963 ± 712	102 ± 16	1609 ± 384	1137 ± 108
αIL-6	1956 ± 216	443 ± 31	643 ± 55	118 ± 53	1522 ± 377	1038 ± 163
αIL-12	2026 ± 316	422 ± 76	7121 ± 1210	22 ± 5	1367 ± 123	1176 ± 253
αTGF-β	1948 ± 402	398 ± 88	6712 ± 938	132 ± 89	1653 ± 277	988 ± 103
αIFN-γ	1895 ± 308	482 ± 45	6357 ± 1305	124 ± 73	167 ± 38	218 ± 37

Supplemental Table 6. Antibodies used in experiments

Antibody	Clone #	Supplier
immunoblotting		
Mouse anti-human Stat1 (Tyr701)	14/P-STAT1	BD Transduction Laboratories
Mouse anti-human Stat1	42/Stat1	BD Transduction Laboratories
Mouse anti-human Stat3 (Tyr705)	4/P-STAT3	BD Transduction Laboratories
Mouse anti-human Stat3	84/Stat3	BD Transduction Laboratories
Rabbit anti-human JNK (Thr183/Tyr185)	98F2	Cell Signaling Technology
Rabbit anti-human JNK	56G8	Cell Signaling Technology
Rabbit anti-human ERK (Thr202/Tyr204)	20G11	Cell Signaling Technology
Rabbit anti-human ERK	137F5	Cell Signaling Technology
Rabbit anti-human P38 (Thr180/Tyr182)	D3F9	Cell Signaling Technology
Rabbit anti-human P38	D13E1	Cell Signaling Technology
Rabbit anti-human AKT (Ser473)	D9E	Cell Signaling Technology
Rabbit anti-human AKT	C67E7	Cell Signaling Technology
Rabbit anti-human IκB (Ser32)	14D4	Cell Signaling Technology
Rabbit anti-human P65 (Ser536)	93H1	Cell Signaling Technology
Rabbit anti-human P65	D14E12	Cell Signaling Technology
Rabbit anti-human Mcl1	D35A5	Cell Signaling Technology
Mouse anti-human Bcl-xl	44/Bcl-x	BD Transduction Laboratories
Mouse anti-human Bcl2	7/Bcl-2	BD Transduction Laboratories
Mouse anti-human BID	7/Bid	BD Transduction Laboratories
Mouse anti-human BAX	3/Bax	BD Transduction Laboratories
Mouse anti-human GAPDH	2D9	Origene
neutralizing		
Human TNF-α Antibody	28401	R&D system
Human IL-1β Antibody	8516	R&D system
Human IL-6 Antibody	6708	R&D system
Human IL-12 Antibody	24910	R&D system
Human TGF-β Antibody	9016	R&D system
Human IFN-γ Antibody	25718	R&D system
mouse experiments		
anti-mouse CD3ε	145-2C11	Bio X Cell
anti-mouse CSF1R	AFS98	Bio X Cell
anti-mouse PD-L1	10F.9G2	Bio X Cell
flow cytometry		
Alexa Fluor 700-conjugated anti-human CD3	OKT3	ebioscience
APC-conjugated anti-human CD56	TULY56	ebioscience
eFluor 450-conjugated anti-human CD15	MMA	ebioscience
FITC-conjugated anti-human CD14	RMO52	Beckman Coulter
PE-conjugated anti-human PD-L1	MIH1	ebioscience
PE-Cy7-conjugated anti-human CD19	J4.119	Beckman Coulter
Krome Orange anti-human CD45	J33	Beckman Coulter
APC-conjugated anti-mouse F4/80	BM8	Biolegend
Brilliant Violet 570-conjugated anti-mouse CD45	30-F11	Biolegend

eFluor 450-conjugated anti-mouse CD8a	53-6.7	eBioscience
FITC-conjugated anti-mouse CD107a	1D4B	ebioscience
PE-conjugated anti-mouse CD3	17A2	Biolegend
PE-Cy7-conjugated anti-mouse CD274	10F.9G2	Biolegend

Suppliers: BD Transduction Laboratories (San Diego, CA); Cell Signaling Technology (Beverly, MA); Origene (Rockville, MD); R&D system (Minneapolis, MN); Bio X Cell (West Lebanon, NH); ebioscience (Waltham, MA); Beckman Coulter (Brea, CA); Biolegend (San Diego, CA).

Supplemental Table 7. Primers for real-time PCR

Gene		Sequences
Human *CDH1*	Forward	CCG CTG GCG TCT GTA GGA AGG
	Reverse	GGC TCT TTG ACC ACC GCT CTC C
Human *VIM*	Forward	GAG AAC TTT GCC GTT GAA GC
	Reverse	TCC AGC AGC TTC CTG TAG GT
Human *CD274*	Forward	CCA CCA CCA ATT CCA AGA GAG A
	Reverse	GGC TCC CAG AAT TAC CAA GTG A
Human *SNAI1*	Forward	GGA TCT CCA GGC TCG AAA GG
	Reverse	GAC ATT CGG GAG AAG GTC CG
Human *SNAI2*	Forward	TGT GTG GAC TAC CGC TGC TC
	Reverse	GAG AGG CCA TTG GGT AGC TG
Human *GAPDH*	Forward	GAG TCA ACG GAT TTG GTC GT
	Reverse	GAC AAG CTT CCC GTT CTC AG
Mouse CD274	Forward	TGC TGC ATA ATC AGC TAC GG
	Reverse	GCT GGT CAC ATT GAG AAG CA
Mouse GAPDH	Forward	AAA TGG TGA AGG TCG GTG TGA AC
	Reverse	CAA CAA TCT CCA CTT TGC CAC TG