**Supplementary Fig. S1.** Kaplan Meier curves of time from diagnosis to detectable distant metastases in dogs with luminal and basal subtype InvUC (StataSE16). In exploratory analyses, the time from diagnosis to the detection of distant metastases was significantly shorter in nine dogs with basal tumors (median 110 days) than in eight dogs with luminal tumors (median 394 days) (P= 0.0113). The findings are considered exploratory because the specific drug protocols differed between cases. The monitoring and staging schedules were similar; no dogs underwent cystectomy nor radiation therapy; and all dogs were treated with drug therapies. Of nine dogs with basal tumors, the initial treatment consisted of intravenous chemotherapy and a COX inhibitor in six dogs, intravesical chemotherapy and a COX inhibitor in one dog, and single agent COX inhibitor in two dogs. Note that COX inhibitors have antitumor activity in dogs with InvUC and are often included in treatment protocols [22]. Of eight dogs with luminal tumors, the initial treatment consisted of intravenous chemotherapy and a COX inhibitor in five dogs, an oral demethylating agent and a COX inhibitor in one dog, and single agent COX inhibitor in two dogs.
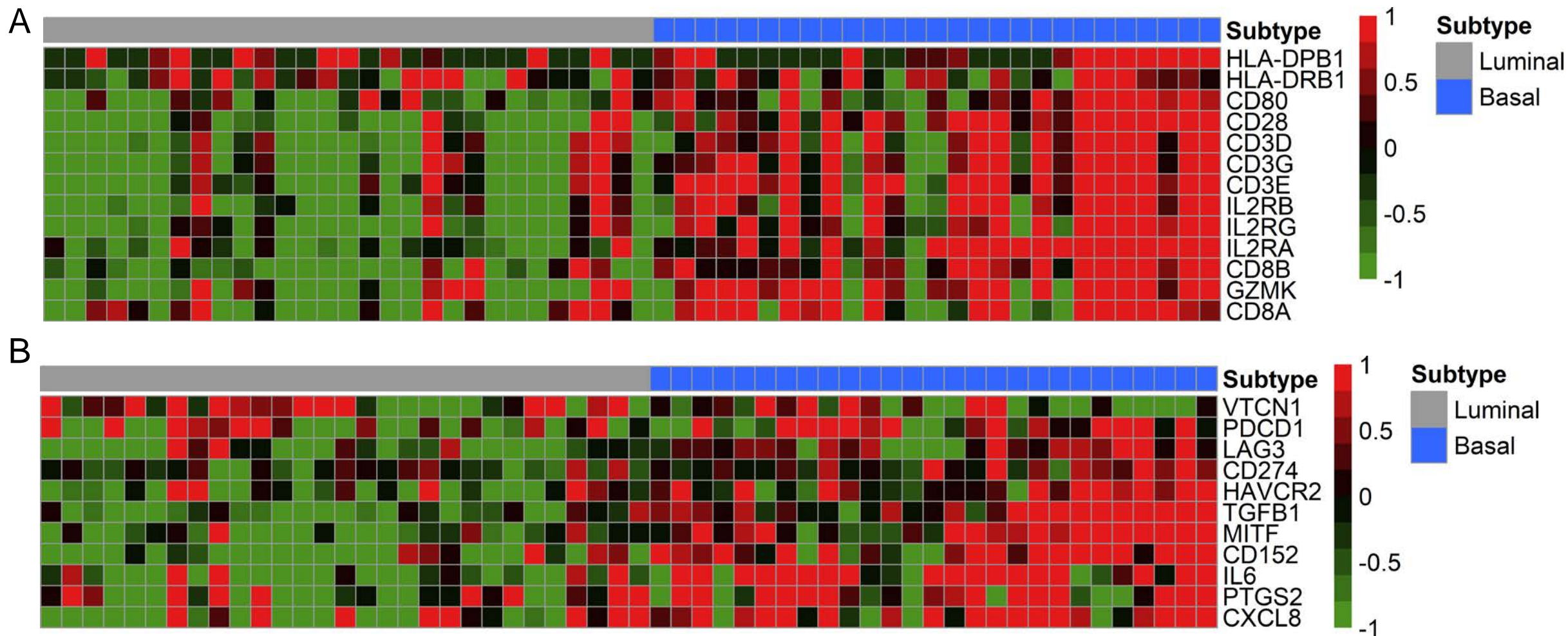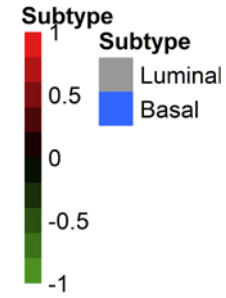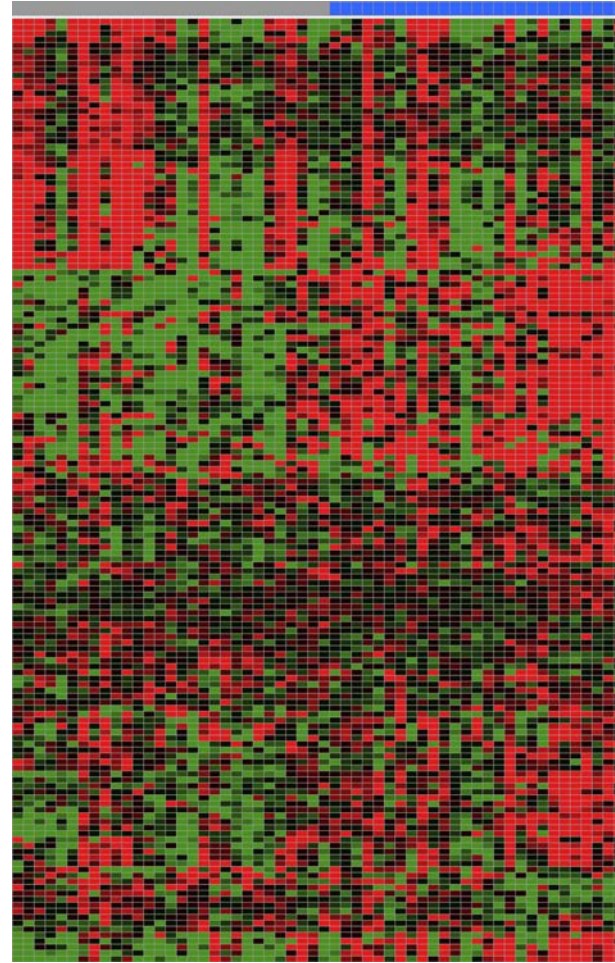
Supplementary Fig. S2. Canine InvUC, RNA-seq analyses of immune genes in luminal and basal subtype cancer. In the heatmap, the luminal and basal subtype tumors (samples with gray and blue column headings, respectively) were defined by class prediction model [21]. The data were interrogated for genes typically involved in enhancing the immune response (upper panel) or in suppressing the immune response (lower panel) to cancer [9, 11, 17, 31, 43, 46]. Note that genes involved in enhancing the immune response and in suppressing the immune response are overexpressed in the basal tumors.
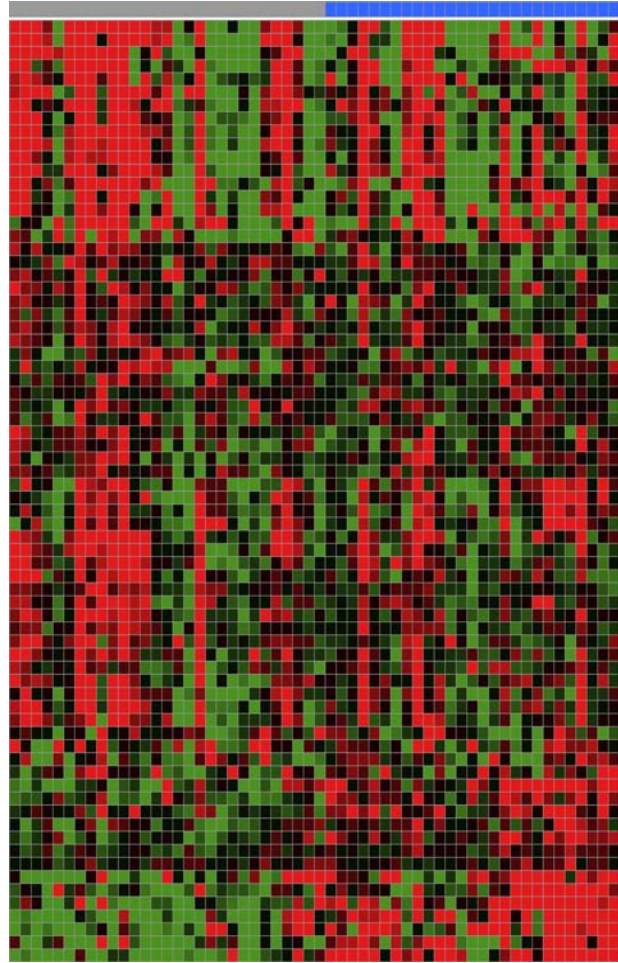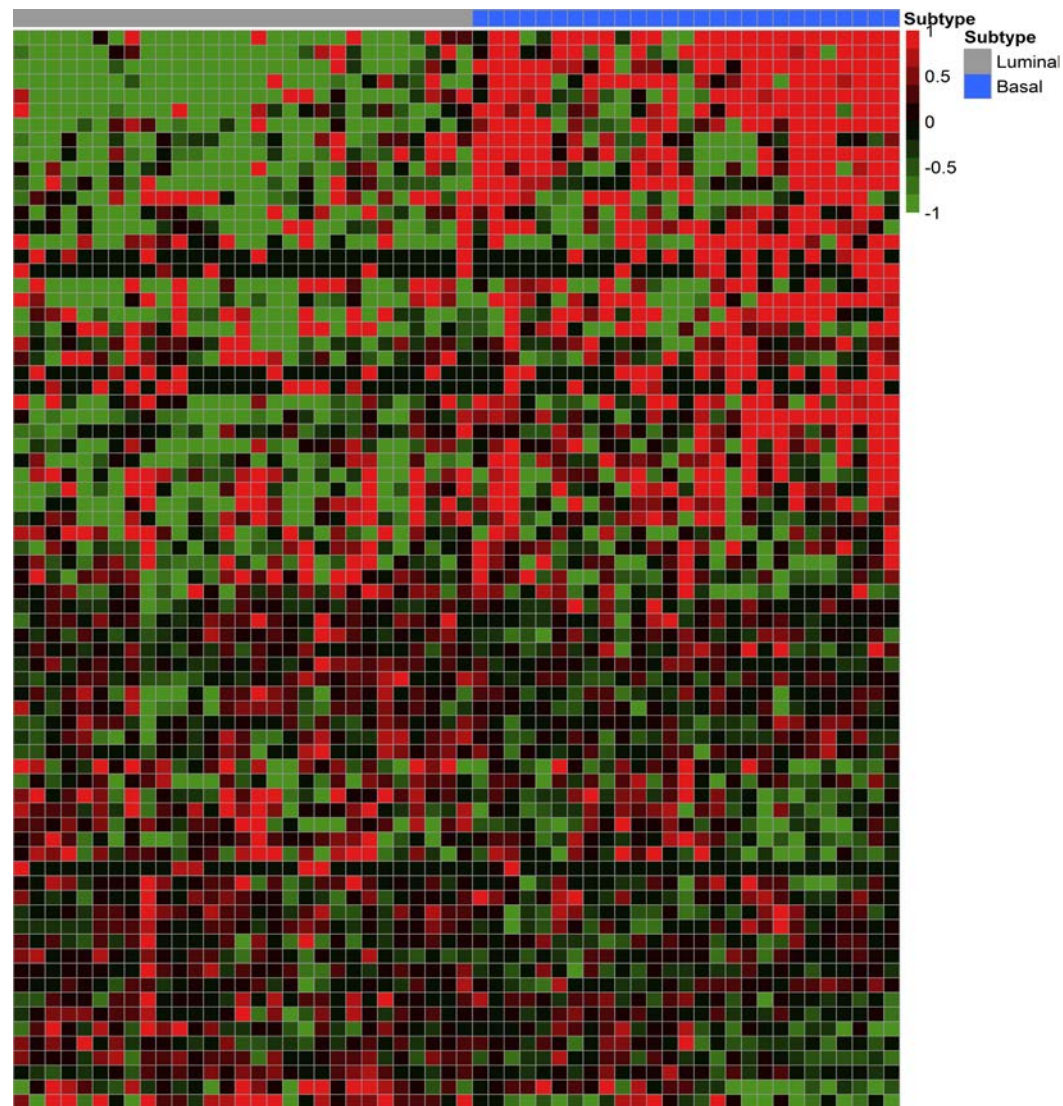
Supplementary Fig. S3. Canine InvUC, RNA-seq analyses of interferon-inducible genes in luminal and basal subtype cancer. In the heatmaps, the luminal and basal subtype tumors (samples with gray and blue column headings, respectively) were defined by class prediction model [21]. Differentially expressed genes identified in canine InvUC were clustered using: **A**. IFNα-inducible genes (n=72), and **B**. IFNγ-inducible genes (n=158) [17, 32], Note the basal and luminal canine InvUC samples are enriched for IFNα and IFNγ-inducible genes. Heterogeneity across samples was observed with enrichment of several IFN-inducible genes in both subtypes. The genes in the heatmap are listed in **Supplementary Table S4A, B**.

Supplementary Fig. S4. Canine InvUC RNA-seq analyses of TGF-β pathway signatures. In the heatmap, the luminal and basal subtype (samples with gray and blue column headings, respectively) were defined by class prediction model [21]. The expression of TGF-β pathway genes (n=74) was determined using KEGG pathway hsa04350 [32]. Several genes were enriched in basal tumors. The genes in the heatmap are listed in **Supplementary Table S5** in the same order as in the heatmap.
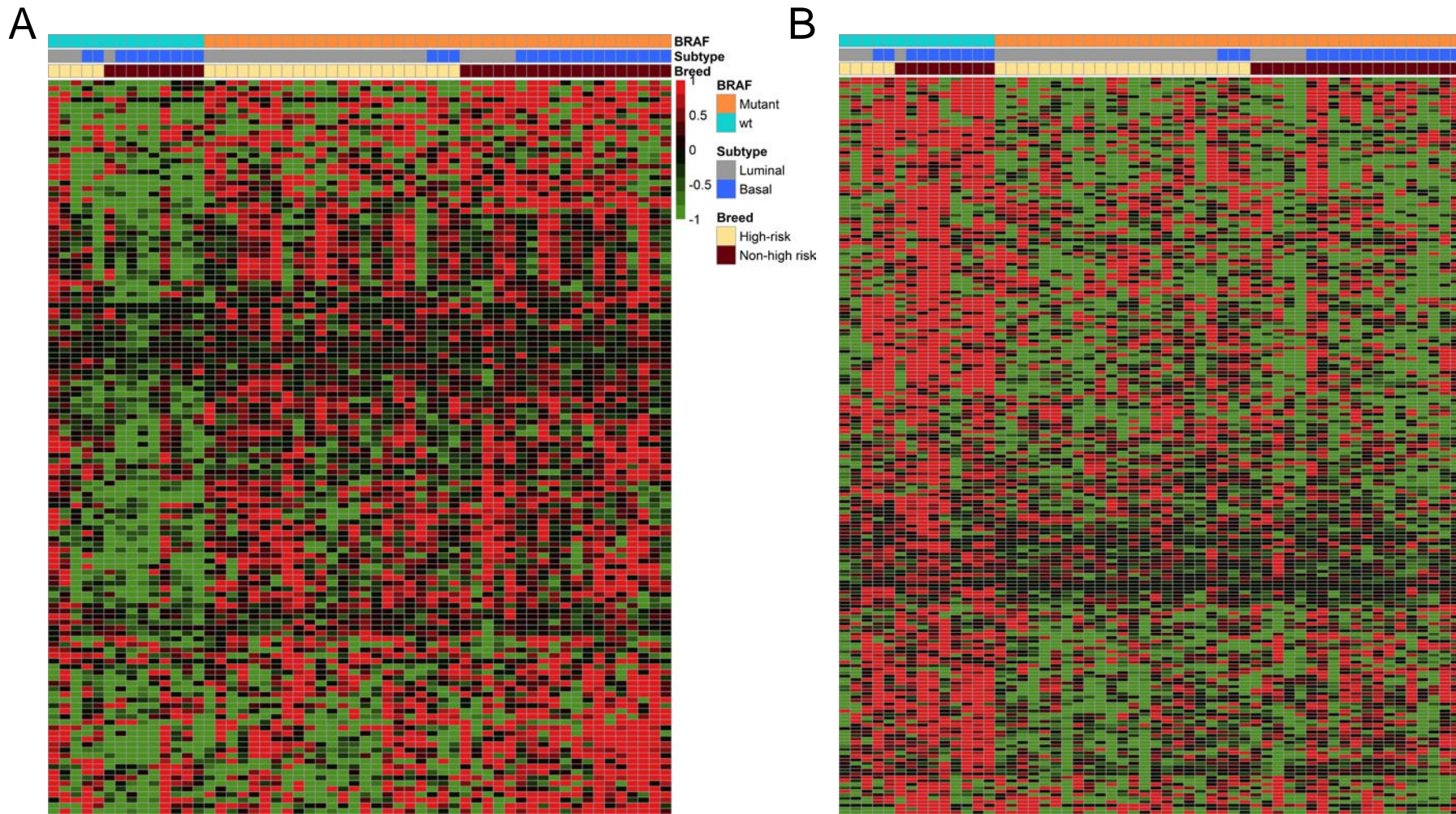
Supplementary Fig. S5. Canine InvUC RNA-seq analyses of a panel of genes previously reported to segregate canine bladder tumors with the *BRAF*^V595E mutation from tumors with wild type *BRAF* [27]. The previously reported gene list was separated into two group: the genes that were enriched in tumors with the *BRAF*^V595E mutation (**A**), and the genes that were enriched in tumors with wild type *BRAF* (**B**). The RNA-seq data was interrogated for the genes in these lists. As previously reported, the genes preferentially enriched in InvUC with *BRAF*^V595E were largely found to be enriched in tumors with the mutation (**A**), and the genes preferentially enriched in InvUC with wild type *BRAF* were largely enriched in tumors with wild type *BRAF* (**B**). Some heterogeneity was noted within these expression patterns, which was expected. The genes in the heatmap are listed in **Supplementary Table S6 A and B** in the same order as in the figure.

Supplementary Table S1. List of genes included in the 60-gene panel used to distinguish luminal and basal tumors in canine InvUC in Fig 1.

MMP9
ACTG2
DES
PRRX1
KIF5C
SERPINE2
DCN
FBLN1
COL1A1
COL1A2
CAV1
RARRES2
ZEB1
AXL
RASA3
RCN3
VIM
TAGLN
ACTA2
MYLK
TPM2
MYL9
LY6E
SCNN1B
CDK3
CLDN3
AGR2
DHRS2
TMEM97
CLDN7
CDH1
GDPD3
SULT1A1
PLEKHG6
SLC14A1
PPARG
GRB7
ERBB2
RNASE1
VGLL1
CAPN5
ELOVL6
UPK3A

FBP1
BCAS1
CYP1A1
CTSE
KCNJ15
LIMCH1
EMP3
FGL2
WAS
CTGF
SOCS3
SERPINA1
PALLD
LYN
TGFBR3
SOX9
TLE2

Supplementary Table S2. List of genes associated with cancer progression in the nCounter® PanCancer Progression Gene Panel in Fig 3.

PRSS8
GZMK
CXCL13
SMOC1
SRPX2
CAV1
FN1
IL11
INHBA
BGN
CYP1B1
GREM1
SFRP2
RELN
KRT14
SOX2
THBS4
MMP3
MMP1
TAL1
GATA4
SPDEF
RPS27A
SEMA3E
IL1RL1
ENPEP
HUNK
FGFR4
DCC
SLIT2
PTX3
AKAP12
FRAS1
BICC1
NOS2
EGF
ADM2
STAB2
OAS1
CST7
GALNT7
SCNN1A

EPHA2
MAPKAPK3
TNFRSF1A
EPHB3
LAD1
TJP3
PPL
EVPL
MMRN2
AGRN
ADAM15
HOXA5
HOXA7
AKT1
SMAD3
EDC3
CBLC
TMC6
OVOL2
RAB25
AP1M2
SH2D3A
ERMP1
RBM47
SLC35A3
CTNNB1
OCLN
TOM1L1
EPS8L1
PLS1
EPCAM
FBLN5
F11R
ELF3
LLGL2
ERBB2
ERBB3
CGN
ESRP1
NDRG1
TMPRSS4
ST14
CLDN7
CDH1
EIF4EBP1
UBA52
CRIP2

SNRPF
GPX1
ADAP1
DESI1
NOL7
ATPIF1
SOD1
WARS
RPS27A
KRT19
SH3YL1
VAMP8
CD82
MTMR14
MAP2K1
AAMP
EGLN3
GPI
SLC2A1
MT3
NDP
HSD17B12
CAMK2D
LY96
NME1
DENR
MAPK1
CDC42
HDAC3
KDM1A
MAP3K7
ITGB1BP1
DDX50
PRPF38A
ZNF143
PDCL3
SKP1
PDCD10
ADAM9
PPP2CB
MTBP
PTK2
HSP90B1
NCL
RHOA
MTDH
HDHD3

TLR4
PRKCZ
CHP1
PPP2R1A
CYB561
HSPB1
GPATCH3
ILK
EIF2AK3
EIF2B4
USP39
PLA2G10
RAF1
AKT2
RPS6KB2
TCF3
PKN1
MAP2K2
BAD
CIB1
RNH1
HRAS
ITGA3
CDKN1A
SRF
SRC
SDC4
BMPR2
SSTR2
PIK3R1
PLCG1
TP53
PNPLA6
ROCK2
TJP2
MYO1D
RAC1
SRPK2
CTNND1
BRMS1
MTOR
PKNOX1
SMURF1
MTA1
ARHGAP32
VAV2
WWTR1

ERCC3
SAP130
NAA15
AMMECR1L
SP1
NFKB1
SETD2
DICER1
CHD4
HIF1A
GTF2I
ZKSCAN5
NF1
TLK2
CNOT4
QKI
SH2B3
PIK3CA
STAT3
NF2
TCF20
ADAM17
KRAS
PTEN
VPS13A
RBPJ
SMAD4
SMAD5
ZFYVE9
ZFYVE16
AGGF1
ARAP2
DLG1
MAP2K4
RBL2
CEP295
CHAD
KRIT1
DHX16
MED23
TRIM39
CD2AP
CASP8
RBL1
SMC3
SERINC5
IRF6

PFKFB4
BTG1
CUL1
AGK
SMAD2
ROCK1
FOXO4
BMPR1A
ZNF346
GRHL2
DAG1
RB1
ADD1
RTN4
ZC3H14
TMUB2
HDAC5
GLYR1
DNAJC14
COG7
NUBP1
SIRT1
MRPS5
CNOT10
MED1
RPS6KB1
VEZF1
SMAD1
SPHK2
CC2D1B
HIPK1
FGFR3
FGFR2
DLL4
AGT
CD36
SLC12A6
SLC44A4
MYO5C
TXNIP
PPFIBP2
EGFR
CDS1
PRR15L
ITGA7
EPN3
SLC37A1

PITX2
FREM2
MYCL
TMPRSS2
FBP1
BCAS1
SORD
ALOX5
MUC1
CLDN4
PRSS22
ZC3H12A
ANGPTL4
FBN2
NDNF
HAPLN1
ITGA8
SFRP1
DPT
TMEM100
COL1A1
COL6A3
COL3A1
COL1A2
COL6A1
LOX
DPYSL3
CCDC80
ADAMTS12
THBS2
TNC
ITGA11
FAP
SERPINF1
C1S
HGF
MMP2
LUM
POSTN
VCAN
FBN1
RORB
COL4A6
DCN
IGF1
KCNJ8
FST

TIMP4
TBX4
NAP1L3
SV2B
TSHR
CDH2
BMPER
VWA2
LHFP
MCAM
MPDZ
TCF4
ZEB1
HEG1
TNS1
NRP1
PLXND1
TGFB1
FXYD6
JAM3
ACVRL1
SYNE1
RORA
GJA5
S1PR1
CD34
EMCN
CALCRL
TEK
ECSCR
PECAM1
KIAA1462
PTPRB
VEGFC
ADAMTS1
FLT1
ROBO4
KDR
PTPRM
NOS3
IGFBP7
MMP14
SNAI2
ASPN
MEOX2
LTBP4
APOD

ECM2
OGN
CRISPLD2
TF
SPARCL1
ANPEP
CTSK
APOE
SMAD9
PLXDC1
SERPING1
CCR2
PPP1R16B
FLI1
ENPP2
CXCR4
CSF2RB
PIK3CG
PLCG2
PTPRC
SAMSN1
RAC2
CLEC2B
GIMAP4
SYK
PIK3CD
PRKCB
HMOX1
TGFBI
WNT5A
HK3
ITGAM
CFP
SERPINA1
IL1RN
CXCR3
CD163
C3AR1
VSIG4
WIPF1
PLXNC1
FGL2
PIK3R6
NFATC2
VASH1
ITGA9
AQP1

SOX17
CDH13
VIT
TNF
COMP
EDN1
SELE
C3
CXCL12
FGF9
LAMA1
VCAM1
BMP5
SPOCK3
ABI3BP
MFAP4
JAM2
PTGDS
PRELP
FMOD
CHRDL1
ADAMTS8
CLEC3B
TPM2
MYLK
MYH11
ACTG2
NCAM1
PTGIS
RAMP1
TBX1
CMA1
EPHB1
TSPAN1
PEBP4
SNAI3
BMPR1B
NRCAM
ID4
TMPRSS6
SRGN
TF
ITGB6
B3GNT3
HOXB3
HOXB13
CLDN3

AGR2
MISP
S100A14
ETV4
EPHA1
PLA2G3
CX3CL1
BMP7
LAMB3
LAMA3
ITGA2
LAMC2
ZFPM2
HK2
DSC2
FREM1
EMILIN3
CLDN1
MMP24
MET
ITGA6
ICAM1
MRC1
NRP2
LRG1
IL18
ARHGDIB
JUN
PDGFC
ADAM28
IL10RA
ADAM8
THBS1
OLFML2B
BMP4
ITGA1
PTRF
TGFB2
NPR1
LOXL2
EPAS1
FGFR1
CEACAM1
PROM1
SOX9
JAG1
ACVR1

CTSH
CADM1
MYC
HPSE
TNFRSF12A
P3H2
TBXA2R
ENO3
NR3C1
ITGB1
CLIC4
DLC1
VEGFB
ENO2
NOX5
IL13RA2
COL5A1
HIPK2
LAMC1
RUNX1
AHNAK
NFAT5
NOTCH1
CREBBP
EP300
PIK3R5
VAV3
CEP170
MGAT5
BAG2
SERPINH1
P3H1
CTSL
CTSL
AKT3
LIFR
FERMT2
HAS1
TIE1
IL15
TGFBR2
ELK3
DENND5A
RRAS
VWA1
CXCL17
EGFL7

PLEKHO1
TNFSF12
TNFSF10
GSN
PTK2B
VEGFA
ANGPT2
EIF4E2
EPHB4
FLT4
MMP12
CD44
CLU
MMP13
GDF15
FOXC2
NODAL
WNT5B
CXCL10
IFNG
PRF1
FASLG
CCL5
CHI3L1
SPP1
POPDC3
SCG2
INHBE
HLA-DPB1
ITGB7
ITGB2
TNMD
HKDC1
CTSL
APOH
GDF5
PLA2G2D
KRT1
ACVR1C
PFKFB1
GDF6
IBSP
ISL1
SPINK5
NTRK1
CCL7
TNN

ALB
CAMP
CCBE1
CTSG
ADRA2B
PDPN
CDH11
PCOLCE
ANGPTL2
DST
ANGPT1
IGFBP4
ZCCHC24
FBLN1
CDK14
COL7A1
PMP22
EMP3
LGALS1
THY1
VIM
ITGA5
SACS
BNC2
EMILIN1
ZEB2
ITGB8
HSPG2
CSPG4
LAMA4
PDGFRB
CALD1
FSTL1
PXDN
DDR2
COL18A1
SPARC
COL4A1
COL4A2
RUNX1T1
COL5A2
ACHE
SNAI1
FGF18
CCR3
CAMK2A
ISLR

FHL1
TWIST2
TIMP1
AREG
TFPI2
MMP9
CXCL8
IL1A
IL1B
CCL8
NR4A1
IL6
PTGS2
SERPINE1
PLAUR
PLAU

Supplementary Table S3. List of genes included in Fig. 5 that have been used to classify human InvUC as T-cell-inflamed.

RHCG
ST6GAL2
SLC6A14
L1CAM
ERMN
HEPH
TMEM130
TNFRSF11B
DHRS9
MYO7B
FLNC
JPH2
CORIN
A1BG
SCG5
STMN3
NCF4
HTRA4
GATA5
ADM2
RAB39B
SLC31A2
MPP1
SGK1
RAB32
FBLN5
RASGEF1B
SLCO4A1
CEBPB
KIRREL
ZMYND15
NUPR1
NXPH3
PRR5L
IGSF21
GBGT1
IL6ST
MYC
DENND3
MYO1B
FCRL6
JDP2

IRAK3
CTSZ
KDELC1
LY96
FRMD4B
AP1S2
CPPED1
CALU
TSPAN4
SH2B3
KLF7
BIRC7
ASPG
ADRB3
KREMEN2
COX7A1
VENTX
S100B
PLN
DBH
CPA4
SLC9A7
CST7
FLVCR2
GDPD5
FZD8
SH3RF3
NR3C1
BIN1
RASSF4
KDELR3
XG
TLR4
ARRB2
ANGPTL6
LAP3
PDE6G
CTSW
OSTM1
TM6SF1
RAB23
FAM26F
RNF130
ECHDC3
NXN
APOL6
RELB

SIGLEC1
ANXA3
CLIC3
MSRB3
CD82
HRASLS5
MFHAS1
SGTB
PTPRJ
VASN
FAM20C
TRIM36
FSTL3
KIFC3
UNC13D
AMOTL2
AKAP12
TBXAS1
F10
HSPB8
ABLIM2
FBXO32
LIF
NFIL3
HBEGF
SOX9
ANXA1
GMPR
SLC7A5
SGMS2
AJAP1
HPSE
PPM1K
IL15RA
OAT
SERPINB1
FAS
WARS
IRF1
PARP11
OPTN
RNF19B
CFLAR
CYBRD1
F2R
OSBPL6
TGM2

PAPSS2
CYP7B1
CYP26B1
ESR1
OSR2
NT5E
EPHB2
TGM1
PIPOX
CALB2
PPFIA2
ANKH
LIPG
FLRT2
RGS2
TNFRSF12A
CLCF1
PRRX2
IGFBP6
SLC16A1
F2RL2
ENOX1
SARDH
XYLT1
ENTPD1
MEIS3
TMEM45A
NPR1
LTBP1
CHST1
SUSD2
SERPINE2
ETV1
ZFPM2
SOBP
PMEPA1
ARHGAP31
RET
SPSB4
RHEBL1
TMEM200B
GALNT6
FBLN7
ST3GAL6
ANTXR2
CAMK1G
LAMA3

GFOD1
TMTC1
CCND2
CX3CL1
SPNS3
SLC2A4
TSPAN32
LGALS2
CDC42EP1
TIFAB
NINJ2
CRYAB
DCBLD2
PSD
TNFSF10
TNFSF12
FLT3LG
TMEM106A
TLR3
ADA
GADD45B
SAT1
VAMP5
TUBB2A
PRKCDBP
GSN
PDGFC
EMP1
RRAS
CST6
MNDA
GREM2
F2RL3
PSTPIP1
TTYH2
STK10
LYN
SPHK1
NEK6
AFAP1
UBASH3B
ELK3
CTSB
IL1RAP
SOD2
RAB27A
STK17A

NCOA7
CYLD
JAK2
KLHL5
SNED1
RHOF
TRIM47
FMNL3
STK32B
IL24
SLC15A3
KCNK3
C19orf35
SOAT1
RCAN1
TEAD4
ANXA5
ITPRIP
TNFRSF1B
FXYD5
BMP1
STOM
IL18BP
ITGB2
SLC11A1
CFP
CREB5
HHIPL1
NRP2
PLEK
CSF2RA
CASS4
C5AR1
LOXL3
MITF
ITGAX
FOLR2
MRC1
SLC39A8
SLC6A9
CYSLTR2
CD80
FYB
FCER1G
HSD17B6
RGS20
DZIP1

LTF
SHC4
ARRDC5
ART3
DACT1
PTGIR
FBLN2
ENPP1
EDNRA
SLCO2A1
AFAP1L2
RASGRF1
LCN2
OLFM1
ISLR2
ADAMTS15
DCLK1
HSPA12B
BICC1
PLS3
NTRK1
P2RX1
HLF
MCHR1
ZNF683
NOS2
FAM69A
SLC24A3
ST6GAL1
SYTL3
PLD4
SUSD3
STAP1
ISG15
RSAD2
ISG20
OAS2
IFIT2
DDX60
IFIH1
HERC6
DDX58
IFI44
IFI44L
XAF1
ZBP1
BST2

MX1
LY6E
IFIT3
IFIT1
SHOX2
SLAMF9
IDO1
CXCL10
TOX2
SCEL
PADI2
DSC2
FGFBP1
LYPD1
BHMT2
LSAMP
GRID1
UBE2QL1
REEP1
NECAB1
SGCD
MMP9
ATP6V0D2
GPBAR1
PCP4
KCNK13
MDGA1
PCBP3
GPRIN3
SLA
PDZK1IP1
EGFLAM
FAM78A
IL1RL1
SRGN
FAM124B
FAM159A
RNASE1
STAC
FAM65C
SLIT2
TCN2
MFAP2
STXBP6
GPM6A
ENPEP
DPP4

BDNF
ELOVL2
ADAM23
MME
CXCL12
DIO3
ABCB4
ANPEP
MATK
GHR
AKAP6
DGKI
RORA
EIF5A2
ITGBL1
UNC5C
APBA2
CCL17
MKX
TMEM200A
VEPH1
TNN
CCL22
CCR8
RAMP1
C16orf89
CPNE5
GLIS1
MAMDC2
CCL14
IQGAP2
LRRN2
CCDC102B
C10orf128
RRAD
UBD
C16orf54
VPREB3
CD52
TBC1D10C
PLAC8
VMO1
DNAJC12
KIAA1324
IDO2
APOC2
P2RX7

GPA33
PPM1J
RNF144B
ALDH1A1
LOXL4
PAQR5
FMN1
DIXDC1
WWTR1
SLC4A8
GABRP
HS3ST2
CPVL
CLEC7A
SLC19A3
PDCD1
TRANK1
SAMD9L
PARP9
PARP14
RARRES3
IFI35
UBE2L6
ETV7
B2M
PSMB8
TAP1
PSMB9
KCNJ12
NEURL3
SFMBT2
P2RY13
GPR171
P2RY14
TNFSF9
CHRNA1
OR51E1
SUCNR1
EVC2
EVC
BEND6
PDE3A
UCHL1
SERPINF2
HAS1
MYOZ3
SAMD3

TAS1R3
PYGM
GPR18
IL13RA2
PTGER2
PRAM1
ADCY9
DPEP2
RECK
MRO
REM1
ZNF114
NLRP3
HELB
FAM46B
VTN
NNMT
BTBD19
SSTR2
GPR141
ME1
GPR176
ALDH1B1
SLC47A1
GLT1D1
TREML1
LRRC2
ACSM5
FMO3
FAM107A
SLC22A4
SLC12A8
ACOX2
NPR3
ITGA7
MGLL
PRPH2
PTGFR
OMD
LRRTM2
COL10A1
SLC16A4
LRRN3
GPR82
SMTNL1
SEMA6B
CHST3

STAC3
TNFRSF6B
RGS9
CDK6
CDC25B
FBXO39
MYOM3
ABCD2
SERPINA3
RFX8
GHRL
RAB33A
MYBPC3
GRIP2
GPR1
SETBP1
GRIN3A
PPP2R2C
SYPL2
SOD3
REEP2
DHH
DDIT4L
GTF2A1L
CLIC2
SLC16A10
TIE1
NTN1
KANK4
PRPH
PLXNA4
UNC5A
TACR1
STX11
MAN1A1
ITGAM
OXCT1
DPYD
CSGALNACT1
COPZ2
PRNP
AKT3
RGAG4
LMCD1
PNMA1
TCF7L1
CAP2

SLC16A2
SERPINB9
RASGRP1
SLC30A4
VNN1
LIFR
ANKRD29
RNASE6
MRAS
FERMT2
GPR155
TCP11L1
TGFBR1
DEPDC7
CORO1C
FSD1L
FKBP5
NMT2
TUBB6
IL27RA
ACOT9
THSD1
SP110
INPP5D
NFATC1
CXCR6
ANKRD44
AKAP5
TMEM140
NFE2
HHEX
KLF9
CYP27A1
HPD
SLC12A3
PODN
FAM129A
CTSG
MPO
MEI1
KLRB1
APCDD1L
BASP1
LZTS1
NEXN
EPHB1
PTX3

SNAP25
LAMA1
KCNK17
SNAI3
HOXD11
EYA1
BMPR1B
MCOLN3
RASSF9
TNFRSF19
PCSK5
PCDH7
GNB4
CRISPLD1
ZDBF2
C2orf40
L3MBTL4
RCAN2
DUSP26
STEAP4
MARCO
ZNF385B
NELL2
NTNG1
SLC6A12
CERKL
OSCAR
ACP5
GPR37
DNAJC5B
NLRP6
PKD2L1
ADORA1
POMC
PTPN5
PHYHIP
ACAN
A2ML1
TMC8
TDO2
GIMAP1
CD74
CIITA
HLA-DRB1
MAP4K1
CD19
FAM19A5

VSTM2L
HCST
HES2
CASQ2
TM6SF2
SLC24A4
PRND
CLDN14
TCEAL7
CDX1
CYTL1
SERPINA5
RNF212
AMZ1
SCN3B
EMILIN2
DOK5
LRRC15
THPO
TNFSF4
IGLON5
CRYBB1
COL6A6
CNGB1
PNOC
NKAPL
CD36
GPR55
RENBP
HMOX1
TRAM2
FMO1
NGF
KCNJ5
FMO2
CRHBP
SLC26A9
CCL26
PATL2
OTOA
KIF19
SUSD5
HECW1
SCG2
LRFN5
KRT9
DCHS2

LRRC55
ZNF804A
CCDC88B
KLK10
NTM
COL11A1
RELN
TBX18
ARSI
SEMA3D
SEMA3A
NAV3
TNFAIP6
THBS4
EYA4
FNDC1
WISP2
SFRP2
GREM1
INHBA
BGN
PRRX1
LTBP2
BBOX1
KIF17
CSMD2
NEFH
NAV2
SLC2A3
WNT11
IBSP
ALOX15B
PTPRN
RGS4
CSF3
NOG
FGF14
PNMA2
AREG
TFPI2
WNT5B
PLAUR
SERPINE1
MT2A
ITGA1
P4HA3
PLAU

MMP11
OLFML2B
CHST15
HAPLN3
MFGE8
GLIS3
SLCO5A1
FAM20A
SYT12
GPR68
PLA2G7
ANXA6
KCNAB2
MMP12
CD109
CAV2
CD44
CREB3L1
GAB3
PLEKHA4
LIMS2
SYNPO
FLNA
IL7
BCAT1
TIMP1
GEM
IGDCC4
CAV1
FKBP10
C1QTNF6
THY1
VIM
ITGA5
COL13A1
NTNG2
GJA4
APLNR
SHANK1
AOC3
SGCA
ADAMTS14
TBX5
ANK2
RASL12
TAGLN
ACTA2

KCNMB1
CD248
CACNA1C
ADAMTS5
MXRA8
FOXL1
FIBIN
BDKRB1
TMEM100
CHRDL2
GAP43
CAMK2A
ISLR
FHL1
FBXL7
TMEM59L
CCDC8
TWIST2
SMOC1
ANKRD1
SERPINB2
PLA2G5
CCL13
CSF2
VAT1L
DKK2
SOCS3
DUSP1
EGR1
EGR2
CH25H
CTGF
CYR61
RGS1
CCL8
CCL2
EGR3
CCL4
CCL3
TREM2
SPP1
CHI3L1
CLEC5A
IL6
OSM
PTHLH
STRA6

IGF2BP2
STC1
NUAK2
LPL
EDIL3
NOX4
SCN1B
TGFB2
TUBB3
GNG11
TBXA2R
BAG2
SNX10
IL15
GLRX
PLAGL1
KMO
CRTAM
KLF12
LATS2
FOXP3
SLC46A3
ADAP2
CD274
CD38
TNFAIP3
IL4I1
HAVCR2
IL12RB2
OGFRL1
KBTBD8
PLXNC1
GPR34
RGS10
RGS18
FGL2
IGSF6
EPB41L3
DOCK4
MYO7A
CHST11
TNFSF13B
HK3
MYO16
CNN3
SLC43A3
ACTN1

ATXN1
ADCY7
CD101
SAMD4A
RASSF3
LRIG1
PGM2L1
ITPR2
CLIC4
ETS1
KIAA0922
SH3KBP1
PDLIM7
DEGS1
CFL2
SGPP1
SLC39A14
STX2
PLEKHO2
GLIPR1
ITPRIPL1
SLA2
SOCS1
CPM
SLC1A4
MATN3
DSEL
PIWIL4
PCOLCE2
BOC
STX1B
ICAM5
PDLIM4
EMP3
LGALS1
ANGPTL1
CDO1
ADRA2A
SLC10A6
IGFBP7
COL8A1
PGR
NTRK3
HMCN1
TSPAN18
MAMLD1
GUCY1A3

GUCY1B3
DOC2B
EBF3
ANK1
SEPTIN6
MYO5A
TPST1
PTRF
MMP3
IL11
MMP1
DSG3
KRT14
WNT7A
CRLF1
GSDMC
TMPRSS3
KRT5
NGFR
NRCAM
RIMBP2
RUFY4
HAMP
IL20RB
GJB2
OLR1
CD177
CEND1
STX19
WNT2
ZNF385D
IFI6
EGFL6
WBSCR17
TNFRSF8
AFF3
AVPR1A
HEPHL1
ATP1A2
ZFHX4
GRIA3
COL8A2
FAM180A
PLA2G2D
CXCR5
CDH2
CILP

GPM6B
ZAP70
RASGRP2
CCR6
KCNA3
SEPTIN1
TRAF3IP3
RHOH
CD69
S1PR4
CLEC2B
CD226
PRKCQ
ITGAL
IKZF1
PRKCB
WDFY4
BTK
CD53
SAMSN1
NCF1
CORO1A
PIK3AP1
AGAP2
CXorf21
LY9
LCP2
SASH3
DOCK2
PTPRC
GIMAP7
CD2
GIMAP4
GIMAP2
AOAH
SLAMF7
TXLNB
GFI1
CCR7
FAM65B
SELL
ARHGAP15
IL16
IL2RG
CD8B
GBP5
GBP6

SLC17A9
IL12RB1
ADORA2A
MEFV
IL1R2
HRH2
PTGDR
KIAA1644
COMP
TNIP3
TNFSF14
TMEM156
CCRL2
DERL3
FFAR2
IL18RAP
CSF3R
TREM1
AQP9
TNF
SCD5
TNFRSF18
TNFRSF4
TNFRSF9
PIM2
BHLHA15
FAM46C
ZC3H12D
SLAMF1
HSPA12A
RBPMS2
IGF2BP3
CHST7
COL12A1
LOXL2
MMP14
GLT8D2
ADCY4
GRK5
OSMR
FOXF1
FGFR1
DPYSL2
GRASP
TGFB1I1
ADARB1
TNS1

SNAI1
ICAM1
PRF1
HIVEP3
THBS1
ADAMTS4
PRDM1
GLIS2
COL5A1
ADAMTS9
LEF1
SELP
VEGFC
OLFML2A
JAM3
STARD8
CYP2S1
NMUR1
SLC18A2
PDE1B
MAP7D3
IL34
NUAK1
KATNAL1
PALLD
SYT11
PLXND1
DSE
PTPRE
TPM1
B4GALNT1
HSPB7
CSDC2
TIAM2
PLCL1
HPGDS
SH2D5
TMCC3
RADIL
MSC
KCNN3
MEOX2
ECM2
OGN
ASPN
PDGFRL
PAPLN

CNRIP1
PLXDC1
JAZF1
GRAMD1B
ARHGAP20
MEOX1
FMNL2
PLXDC2
CACNA2D1
GULP1
LYVE1
RASGRF2
RCSD1
SPOCK2
PPP1R16B
SYNE1
CNTLN
RUNX1T1
TMEM26
PID1
EPB41L2
AXL
RGL1
SLC8A1
ZEB2
RASA3
ST8SIA4
ELMO1
RASSF2
PIK3CD
APBB1IP
CELF2
SGIP1
ADAMTSL4
KIAA1614
ADAMTS10
GAS6
RHOJ
COL5A3
WSCD1
BCL6B
RASGRP3
DYSF
PCDH12
CD93
KIAA1462
ZNF366

GJA5
S1PR1
CD200
CALCRL
SHE
TEK
ECSCR
PECAM1
SH2D3C
EBF1
ZNF521
IL33
MCTP1
NRP1
TCF4
ZEB1
ROR1
CFI
PLK2
KCNE4
CTHRC1
PRSS23
SAMD14
LYL1
RAB37
ADAMTS6
TRPS1
CD70
ST6GALNAC5
AMPH
EBI3
CXCR3
FAM167A
PTAFR
PPEF1
IL21R
HDAC9
MEF2C
KLHL6
DENND5B
ICOS
PDCD1LG2
PTPN7
IRF8
HVCN1
MARCHF1
WAS

TFEC
PLCL2
MYO1F
PLCB2
CYTH4
FERMT3
NCKAP1L
PARVG
VAV1
GPR65
EVI2B
DOCK10
GNG2
FAM49A
SLC9A9
ARHGEF6
ZCCHC24
RAB3IL1
RUNX3
FMNL1
JAK3
CSF2RB
PIK3CG
ACAP1
GRAP2
SPN
SLC16A6
NOD2
FLT3
TNFRSF17
ARHGAP25
ITGB7
KLRD1
MMP25
PIK3R5
GAS7
PODNL1
P2RY6
OR51E2
LRP1
HEG1
DNAJB5
ATP8B2
UBE2E2
FXYD6
HLX
MSN

COTL1
GLIPR2
PIK3R6
FGD2
ARHGAP4
GPR132
GPSM3
MAPRE2
ACVRL1
PREX1
TRPV2
ITGA9
AKNA
IFFO1
TNFSF8
WIPF1
IL10
GIMAP8
SLC7A7
DOK2
DRAM1
DAB2
VASH1
GMFG
IL7R
LCP1
RASAL3
ARHGAP30
PLA1A
LAYN
NFATC2
GALNT10
TRAF1
BMP2K
ADPRH
ST3GAL2
RAB30
IFI30
DENND1C
TLR7
PLEKHO1
LIPA
DPF3
IL18R1
SYDE1
PABPC5
ARNTL2

PLSCR4
ADAM19
FYN
TSPAN11
PRSS35
ANGPT1
COLEC12
FILIP1
FAM198B
RIN3
ZBTB46
RBMS3
PRKG1
DKK3
FSTL1
PDGFRB
PCDH18
SPARC
COL4A1
COL4A2
COL15A1
LAMA4
CALD1
MRVI1
NID1
PXDN
ENG
DDR2
COL5A2
COL18A1
EHD2
ADAMTS2
OLFML3
ANGPTL2
PRICKLE1
LIX1L
RFTN1
RCN3
MRC2
EMILIN1
CDH11
PCOLCE
EFEMP2
SCARA3
FADS3
HTRA1
CDK14

RAB31
SACS
ARHGAP24
MMD
SLC41A2
FAM126A
LHFP
RASSF8
FGF1
CPNE8
KITLG
STARD13
LRRK2
MAP1B
MAP1A
SSC5D
PRICKLE2
LOX
PRR16
BNC2
ARHGAP22
FILIP1L
CCIN
ST8SIA1
ANTXR1
SERPING1
FLI1
ENPP2
TMEM176B
TMEM176A
ITGA4
EMB
PTPN22
CD300LB
SH2D1B
CDA
SERPINA1
C1orf162
LAG3
GPR84
PTPRO
CLEC12A
TMEM150B
CD244
CLEC4E
TLR2
ATP8B4

CD86
IL10RA
PARP15
CARD9
NFAM1
MFSD7
SPI1
IL18
TNFAIP8L2
CD37
SIRPB2
DOK3
HCK
LPXN
CECR1
HCLS1
CD180
LAPTM5
CD48
CASP4
CCR5
FUT7
KCTD12
ARL4C
CX3CR1
GAL3ST4
SLCO2B1
CMKLR1
MFNG
GNGT2
ABI3
ARID5A
FGR
SELPLG
APOC1
APOE
ALOX5AP
ADAM28
SLC2A5
MSR1
NCR3
ADORA3
AIF1
CTSS
TMEM173
CSF1R
MPEG1

TYROBP
TLR8
C1QA
C1QB
C1QC
VSIG4
KLRG1
C3AR1
CD163
LRRC25
MS4A7
GPNMB
C19orf38
CTSK
CD84
CD68
CSF1
FAM129C
KLHL4
CD1D
MAOB
FCER1A
BCHE
HSD11B1
TGFBI
TCTEX1D1
CD1C
BIRC3
CD40
CXCR4
CD83
BIN2
GPR183
TAGAP
LAT2
IL6R
DOCK11
KYNU
SNX20
LYZ
BATF3
TLR6
TLR1
LY86
TLR10
APOBEC3H
CYSLTR1

TMEM71
TRIM69
DNASE1L3
TRIM22
NLRC5
SAMHD1
PDE4B
STK17B
IL2RA
CYTIP
C1QTNF2
S1PR3
CHRD
LTB
LBH
ICAM4
BATF2
C10orf10
CD1E
CCDC69
POU2F2
CD22
CD72
ZBED2
CYP1B1
RGMA
PI15
FBN2
HAS2
NRG1
SLC38A5
PAPPA
FN1
POSTN
ADAM12
IGFBP5
ADAMTS12
ALDH1L2
THBS2
ITGA11
TNC
DAAM2
FAT4
VCAN
LAMA2
MXRA5
COL16A1

IL1R1
HIC1
LRRN4CL
A2M
PMP22
CLEC11A
CERCAM
GAS1
WDR86
PNMAL1
LGI2
CCBE1
CNTN1
ADAMTSL1
DRP2
DTNA
PDZRN4
TRPC3
KCNMA1
PRUNE2
MYLK
TPM2
MYL9
SORCS2
NRXN2
MN1
SYNM
SORBS1
MMRN1
CLEC4G
HLA-DPB1
SNCA
NFIX
SPEG
HTRA3
MRGPRF
ELN
ADCY5
TSHZ3
GLI1
GLI2
FAIM2
GXYLT2
PDZRN3
OLFML1
FXYD1
TMEM119

RARRES2
C1R
C1S
COL1A1
COL6A3
COL3A1
COL1A2
COL6A1
DPYSL3
CCDC80
SERPINF1
FBN1
MMP23B
KIF26B
SCARF2
MYOCD
THSD7A
HSPB6
CLIP3
NDN
NEGR1
CPXM1
CPZ
TRIL
MS4A2
CPA3
RTN1
HDC
TLL1
KIF26A
TNIK
ADAM33
IL3RA
ADAMTS16
PTGS1
PROS1
CRISPLD2
SPARCL1
TRPC4
PDE1A
PEG3
IGF1
ISM1
SPON1
VCAM1
WISP1
PHEX

LPAR4
XPNPEP2
LRRC17
JAM2
MFAP4
PGM5
PDLIM3
PDPN
MMP2
LUM
HGF
FAP
DPT
SCARA5
GFPT2
DCN
EFEMP1
SVEP1
LSP1
ROR2
PKDCC
FST
ADCY2
TGFB3
TSPAN2
GCNT1
MOXD1
DPEP1
ACTC1
RSPO3
PI16
BVES
MYH11
SYNPO2
ACTG2
DES
CLEC3B
GNAO1
ZBTB16
ABI3BP
FMOD
PTGDS
C7
COL14A1
PRELP
NTRK2
NCAM1

PTGIS
AGTR1
CADM3
PTN
COL4A4
COL4A3
MMP16
RYR2
FAM110B
NAP1L3
SPOCK1
HAND2
CLSTN2
F13A1
DOK6
PCSK1
PTPRD
CHRDL1
LRCH2
PRDM6
EPHA3
ADAMDEC1
SFRP4
SMOC2
CPXM2
GZMA
GZMB
GZMK
ZNF831
MOV10L1
CCR2
CCR4
SH2D2A
CCL5
TBX21
SIT1
KLRK1
TRAT1
CD8A
EOMES
CD7
IL2RB
CD96
THEMIS
CD28
SCML4
CD6

CD5
CD27
JAKMIP1
LAT
RAC2
CAMK4
TOX
SH2D1A
CD3D
CD3G
CD3E
UBASH3A
FASLG
LCK
ITK
NLRC3
IKZF3
P2RY10
BLK
BTLA
BACH2
TIGIT
ALPK2
LAX1
SAA1
SELE
IRF4
C15orf48
S100A8
S100A12
EDN1
IL1A
IL1B
MMP7
PI3
C3
CCL20
POU2AF1
CXCL13
CD79B
FCRLA
MS4A1
CD79A
SLAMF6
FGF7
GFRA2
SLC22A3

FEZ1
ADAMTSL3
ABCC9
KCNJ8
MFAP5
CNTNAP1
COL23A1
SFRP1
KIAA1755
NALCN
SV2B
RGS13
CCL19
FCRL5
ASB2
KCNQ5

Supplementary Table S4A.
List of IFNα-inducible genes
in **Supplementary Fig. S3**
ISG15
RSAD2
LY6E
IFIT3
IFIT2
DDX60
IFIH1
DHX58
IFI44
IFI44L
OAS1
HERC6
ISG20
BST2
MX1
CXCL10
GMPR
OGFR
TRIM26
IL4R
PNPT1
TDRD7
TRAFD1
TRIM25
PARP12
CASP8
CD47
LAP3
PSMA3
CNP
NMI
WARS
IRF1
TMEM140
NUB1
B2M
PSMB8
TAP1
PSMB9
IFI35
TRIM14
UBA7
UBE2L6

PSME1
PSME2
IRF9
TRIM21
ADAR
LGALS3BP
MOV10
SAMD9L
EIF2AK2
PARP9
PARP14
TXNIP
CD74
CSF1
IL15
LPAR6
RIPK2
IFI30
SP110
NCOA7
IRF2
ELF1
PROCR
FAM46A
IL7
SELL
CCRL2
BATF2
C1S

Supplementary Table S4B.
List of IFNγ-inducible genes
in **Supplementary Fig. S3**
ISG15
RSAD2
HERC6
IFIH1
TDRD7
TRAFD1
PARP12
TRIM25
ZNFX1
APOL6
PNPT1
SAMD9L

EIF2AK2
PARP14
UBE2L6
PSME1
PSME2
IRF9
TRIM21
MYD88
LGALS3BP
TAPBP
IFI35
TRIM14
IFIT2
DDX60
MX2
IFI44
IFI44L
DHX58
DDX58
RNF213
OAS3
ISG20
OAS2
XAF1
ZBP1
BST2
MX1
LY6E
IFIT3
IFIT1
TNFAIP6
VCAM1
SSPN
C1R
C1S
IL7
BANK1
GCH1
ARL4A
SOCS1
BATF2
SELP
SERPING1
ICAM1
CMKLR1
NLRC5
SAMHD1

PDE4B
GBP6
CD40
SLAMF7
ST8SIA4
LCP2
CSF2RB
IL18BP
MT2A
SOCS3
CCL2
IRF4
PTGS2
IL6
CCL7
IDO1
CXCL10
PFKP
ADAR
PML
ARID5B
FAS
IL4R
CDKN1A
NOD1
BTG1
PELI1
LATS2
TNFAIP3
RIPK2
CD274
CD38
VAMP5
SOD2
JAK2
NMI
IRF2
PTPN1
NFKB1
HIF1A
STAT3
TOR1B
MVP
RIPK1
ISOC1
LAP3
PSMA3

PSMB2
NAMPT
SPPL2A
PLA2G4A
CASP3
BPGM
CASP8
NUP93
PTPN2
GPR18
ITGB7
NFKBIA
CD74
CIITA
HLA-DRB1
IL15
PNP
IL15RA
WARS
IRF1
IRF8
PTPN6
IRF5
IFI30
TNFSF10
EIF4E3
SP110
IL10RA
CD86
CASP4
FGL2
CASP7
B2M
PSMB8
TAP1
PSMB9
P2RY14
AUTS2
METTL7B
TNFAIP2
VAMP8
TRIM26
RBCK1
OGFR
TXNIP
ST3GAL5
NCOA3

GZMA
KLRK1
CCL5
IL2RB
CD69

Supplementary Table S5. List of
TGF-β pathway genes in
Supplementary Fig. S4.
GREM1
INHBA
FBN1
FMOD
RGMA
TGFB3
CHRD
BMP5
DCN
FST
SMAD9
HAMP
BMPR1B
ID4
NODAL
NOG
GDF6
IFNG
TNF
INHBE
ACVR1C
TGFBR2
ACVR1
GREM2
INHBC
TGFB2
TGFB1
TGFBR1
BMP4
THBS1
BMP7
LTBP1
BAMBI
THSD4
AMHR2
ID3
BMP2
BMPR2
ACVR2A
ROCK1
SMAD2
RBL1
SMURF1

RPS6KB1
ZFYVE9
CREBBP
EP300
SMAD5
SMAD4
ZFYVE16
MYC
TGIF2
ACVR2B
SMAD3
ACVR1B
SMAD7
SMAD6
GDF5
PPP2CB
RHOA
SKP1
PPP2CA
RPS6KB2
E2F4
PPP2R1A
SP1
SMAD1
CUL1
E2F5
BMPR1A
PPP2R1B
MAPK1
NEO1
PITX2

Supplementary Table S6A. List of genes enriched preferentially in InvUC with $BRAF^{V595E}$. The genes are listed in the same order as they appear in **Supplementary Fig. S5**.

SLC10A2
SYT1
L1CAM
ENSCAFG00000037584
SPINK4
EFHD1
ALDH1A3
B3GNT7
AREG
ENSCAFG00000036285
GCNT3
PRRG3
NTF4
BEND4
ENSCAFG00000040275
KCNQ4
VGLL3
MYRF
ADGRL4
TGM2
OSBPL6
MTCL1
CYBRD1
BNIP3
DSCC1
DCK
FANCM
MTFR2
FANCI
CHEK1
PCNA
RAD51AP1
KIF20A
MELK
CENPN
FANCD2
CDC25B
CLIP2
MTHFD1L
LMNA
GP1BB

ENSCAFG00000010051
YBX3
SERBP1
IMPDH2
AP3S1
ADSS
KIZ
DYM
cfa-mir-330
SEC31A
NUP93
FANCC
CBFB
MTHFD1
NDC1
LRP8
HAT1
CEP76
PSMG2
MSH2
FOXN2
ENSCAFG00000030498
ENSCAFG00000012233
TKT
TUBA4A
CAPN2
DUSP6
ELK3
PKMYT1
CYB5R3
P4HA2
OSGIN1
PKP1
F2R
GPX7
MTSS1
IMPA2
MBOAT1
KCTD14
BAG1
QSOX1
PLA2G4A
TMTC1
BACE2
LDLR
GPAT3
ERRFI1

CLCF1
GPD2
ACVR1
CCND2
PEX11A
BTBD11
ZFP36L1
SNX9
PTPRJ
SAMD4B
SOS2
PPP1R13B
ENSCAFG00000036184
ENSCAFG00000031625
COL10A1
ZBTB7C
ENSCAFG00000038385
GABBR2
ENSCAFG00000039562
FLRT2
SEMA7A
SEPT5
ANTXR2
ENTPD1
ST3GAL6
LTBP1
SLCO2A1
EVX2
MST1R
GPRC5A
GJB5
FHL2
ANXA1
GJB3
FOXC2
AGPAT4
CD44
SLC12A2
SYBU
SH3BP4
SHOX2
S100A8
SLC16A1
SUSD2

Supplementary Table S6B. List of genes enriched preferentially in InvUC with wild type *BRAF*. The genes are listed in the same order as they appear in **Supplementary Fig. S5**.

CAPS2
GLIPR1L2
CCDC3
ENSCAFG00000025443
FGF10
VIPR2
ZNF831
JAKMIP1
EOMES
ZAP70
KCNQ2
GDNF
HPX
MSTN
MUC15
S1PR5
CD177
ENSCAFG00000032943
TNNI3
CFAP69
ENTPD2
KIF12
AANAT
ENSCAFG00000038334
PLCH2
P2RY1
ENSCAFG00000033758
WNT6
ENSCAFG00000040232
NRCAM
POU6F2
SYCE1
ENSCAFG00000005986
GABRB1
LRRC7
FGF9
UPK1B
TDRD9
REEP1
TMEM200A
ADCY8
SPTBN5

CYP4F22
CCNA1
SLC6A11
ANKMY1
ENSCAFG00000028985
ZNF488
SULT4A1
ENSCAFG00000033428
GJB6
TRAM1L1
GLB1L3
SNAP91
EIF5A2
WHRN
TSPAN33
INSL6
BASP1
ENSCAFG00000038921
SH3GL2
CRYM
CAPN11
GM2A
TTC12
RNF152
GPX3
ASB5
SYT5
ENSCAFG00000031334
SLC16A11
PLA2R1
ALOX12
ENSCAFG00000033839
LRRC6
EFCAB1
FAM110B
TNFRSF19
MAGEL2
MRAP2
CNTNAP1
WSCD2
SLIT3
ENSCAFG00000040777
MAP2K6
FCER1A
ENSCAFG00000039030
ZC3H12C
ZNF608

CPZ
IQCD
ENSCAFG00000004983
HPGD
NAALADL2
TMEM229A
XAF1
MB21D1
ENSCAFG00000035238
VMO1
ENSCAFG00000040164
GLTPD2
DRC1
TF
LPAR3
MRPS34
PNPLA3
MORN3
FBXL13
LRRC56
UBXN11
GATA2
ENSCAFG00000035163
SBK1
KSR1
PIK3R1
ZHX3
PPP2R2B
VWA7
ENSCAFG00000030029
TLE2
SLC40A1
SLC2A5
RBM11
LRIF1
ZNF684
SLC12A6
LGR4
ACAA1
CCDC189
TEF
ZNF316
ACSM3
MB
NTN5
ENPP5
TRAK1

PFKFB4
STK11IP
NUDT18
WBP1
DGUOK
GALT
MSRB2
LINS1
ENSCAFG00000002375
ENSCAFG00000026604
ENSCAFG00000036793
SLC16A13
PLA2G6
PRPF40B
HOGA1
CHD5
COL9A2
HRC
FRMPD1
ENSCAFG00000034860
ENSCAFG00000032089
ENSCAFG00000034931
ENSCAFG00000034948
KCNG3
ENSCAFG00000039838
CATSPERD
CFAP70
HSD17B6
CD70
ENSCAFG00000007045
LTF
SHC4
ZFR2
MYH7
ENSCAFG00000036856
SIT1
TIMD4
CLEC12A
TRIM22
B2M
CD40
CYTH4
CCR5
HEMGN
ENSCAFG00000002042
ENSCAFG00000019771
ZNF677

ADAMTS13
TNNC2
ZNF396
TF
FAM105A
ADGRB2
DOK2
HAVCR2
PARP15
PLEKHB1
KCNN3
ARHGAP45
THEM5
EXD1
ADCY1
BRSK1
DPYSL5
KAZALD1
SLC22A1
RUNDC3A
LHFPL4
TSPAN15
ST6GALNAC2
TRPV6
SGCG
NPY
FAM169A
LSAMP