Supplementary Table 1. List of Upregulated Genes in the MTV High Group Compared to the MTV Low Group (fold change >1.5 and p<0.05)

Gene name (symbol)	Gene bank Accession	Description	Fold change	p-value
H19	BF569051	H19, imprinted maternally expressed transcript (non-protein coding)	6.136	0.044
TMC8	AI370364	transmembrane channel-like 8	1.941	0.033
SPRR1A	NM_005987	small proline-rich protein 1A	1.887	0.046
GJB2	M86849	gap junction protein, beta 2, 26kDa	1.838	0.047
PKP1	NM_000299	plakophilin 1 (ectodermal dysplasia/skin fragility syndrome)	1.757	0.023
SP3	AW470841	Sp3 transcription factor	1.71	0.023
HIST1H4L	NM_003546	histone cluster 1, H4l	1.589	0.008
SNPH	NM_014723	syntaphilin	1.588	0.044
MMP28	BC002631	matrix metallopeptidase 28	1.58	0.043
KYNU	BC000879	kynureninase (L-kynurenine hydrolase)	1.564	0.007
APOL1	AF323540	apolipoprotein L, 1	1.56	0.012
PYCR2	AL561868	pyrroline-5-carboxylate reductase family, member 2	1.559	0.037
TNK2	AI146308	tyrosine kinase, non-receptor, 2	1.554	0.049
METTL8	BC025250	methyltransferase like 8	1.517	0.001

MTV, metabolic tumor volume.

Supplementary Table 2. List of Downregulated Genes in the MTV High Group Compared to the MTV Low Group

Gene name (symbol)	Gene bank Accession	Description	Fold change	p-value
C6orf58	AI857688	chromosome 6 open reading frame 58	0.048	0.002
ACTG2	NM_001615	actin, gamma 2, smooth muscle, enteric	0.079	0.005
TFF2	NM_005423	trefoil factor 2	0.11	0.015
LYZ	AV711904	lysozyme (renal amyloidosis)	0.114	0.011
MYH11	S67238	myosin, heavy chain 11, smooth muscle	0.141	0.012
PGC	NM_002630	progastricsin (pepsinogen C)	0.153	0.024
AGR2	AF088867	anterior gradient homolog 2 (Xenopus laevis)	0.157	0.008
MYH11	NM_022870	myosin, heavy chain 11, smooth muscle	0.166	0.01
PGC	BC042578	progastricsin (pepsinogen C)	0.19	0.033
MYH11	AI889739	myosin, heavy chain 11, smooth muscle	0.196	0.011
LYZ	U25677	lysozyme (renal amyloidosis)	0.209	0.01
DES	NM_001927	desmin	0.21	0.008
PDK4	AV707102	pyruvate dehydrogenase kinase, isozyme 4	0.239	0.046
SYNM	AK026420	synemin, intermediate filament protein	0.248	0.008
MUC6	AI611214	similar to Mucin-6 precursor (Gastric mucin-6)	0.252	0.009
ELN	AA479278	elastin	0.259	0.021
MYLK	NM_005965	myosin light chain kinase	0.345	0.031
MUC3A	AF113616	mucin 3A, cell surface associated	0.357	0.03
SYNPO2	AL552450	synaptopodin 2	0.363	0.039
MFAP4	R72286	microfibrillar-associated protein 4	0.365	0.027
KCNE3	AF302494	potassium voltage-gated channel, Isk-related family, member 3	0.413	0.03
FXYD6	NM_022003	FXYD domain containing ion transport regulator 6	0.422	0.002
KCNE3	AI692703	potassium voltage-gated channel, Isk-related family, member 3	0.486	0.024
FOXF1	NM_001451	forkhead box F1	0.504	0.022
TST	D87292	thiosulfate sulfurtransferase (rhodanese)	0.504	0.029
DPT	AI146848	dermatopontin	0.507	0.004
TSC22D3	AL110191	TSC22 domain family, member 3	0.516	0.026
PCDHGA1	AF152318	protocadherin gamma subfamily A, 1	0.537	0.034
NFKBIA	AI078167	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	0.544	0.039
ALOX5AP	NM_001629	arachidonate 5-lipoxygenase-activating protein	0.55	0.022
MLPH	NM_024101	melanophilin	0.556	0.023
VAPA	AF154847	VAMP (vesicle-associated membrane protein)-associated protein A, 33kDa	0.558	0.049
PLN	M60411	phospholamban	0.558	0.032
DUSP3	AL048503	dual specificity phosphatase 3	0.56	0.044
CMBL	AA209487	carboxymethylenebutenolidase homolog (Pseudomonas)	0.564	0.034
ZNF592	NM_014630	zinc finger protein 592	0.564	0.011
SYNPO2	AI634580	synaptopodin 2	0.573	0.046
HIPK2	R37104	homeodomain interacting protein kinase 2	0.583	0.036
TMED4	AK074557	transmembrane emp24 protein transport domain containing 4	0.586	0.032
RASSF5	BC004270	Ras association (RalGDS/AF-6) domain family member 5	0.587	0.043
LY6E	NM_002346	lymphocyte antigen 6 complex, locus E	0.592	0.014
GNA11	M69013	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	0.596	0.018
CPT1A	NM_001876	carnitine palmitoyltransferase 1A (liver)	0.611	0.009

Supplementary Table 2. Continued

Gene name (symbol)	Gene bank Accession	Description	Fold change	p-value
UTRN	N66570	utrophin	0.616	0.038
TMEM50B	N51405	transmembrane protein 50B	0.622	0.036
CRELD1	NM_015513	cysteine-rich with EGF-like domains 1	0.623	0.013
MAN2C1	NM_006715	mannosidase, alpha, class 2C, member 1	0.624	0.013
CNOT6L	AW514857	CCR4-NOT transcription complex, subunit 6-like	0.625	0.044
ELL2	AI924426	elongation factor, RNA polymerase II, 2	0.626	0.042
ETS2	AL575509	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	0.632	0.017
LOC151162	AL134724	hypothetical LOC151162	0.635	0.046
TADA2B	AI859834	transcriptional adaptor 2 (ADA2 homolog, yeast)-beta	0.635	0.001
LTBP4	NM_003573	latent transforming growth factor beta binding protein 4	0.637	0.002
AKR1C2	M33376	aldo-keto reductase family 1, member C2	0.645	0.05
PCDHGA1	AK026188	protocadherin gamma subfamily A, 1	0.645	0.002
ETS2	NM_005239	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	0.647	0.016
SFRS14	AV738039	splicing factor, arginine/serine-rich 14	0.649	0.037
SLC12A2	AK025062	solute carrier family 12 (sodium/potassium/chloride transporters), member 2	0.65	0.022
LOC338799	AW138760	hypothetical LOC338799	0.651	0.014
HPGD	U63296	hydroxyprostaglandin dehydrogenase 15-(NAD)	0.651	0.031
MAF	NM_005360	v-maf musculoaponeurotic fibrosarcoma oncogene homolog (avian)	0.651	0.044
EIF1B	NM_005875	eukaryotic translation initiation factor 1B	0.658	0.015
PDXDC1	AK025504	pyridoxal-dependent decarboxylase domain containing 1	0.66	0.016
SNW1	NM_012245	SNW domain containing 1	0.661	0.015

MTV, metabolic tumor volume.

Supplementary Table 3. Significantly Upregulated Canonical Pathways in $MTV_{2.5}$ High Tumor Samples

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
B Cell Development	4.53E+00	1.11E-01	NaN	HLA-DQA1, IGL, IGHM, IGHD
Hepatic Fibrosis/Hepatic Stellate Cell Activation	4.39E+00	3.74E-02	NaN	MET, COL12A1, IGFBP3, COL10A1, MYH11, COL11A1, COL17A1
Hematopoiesis from Pluripotent Stem Cells	4.03E+00	8.33E-02	NaN	IGL, IGHM, IGHG1, IGHD
Primary Immunodeficiency Signaling	4.00E+00	8.16E-02	NaN	IGL, IGHM, IGHG1, IGHD
LXR/RXR Activation	3.47E+00	4.13E-02	NaN	APOL1, SCD, LYZ, LPL, PTGS2
Caveolar-mediated Endocytosis Signaling	3.37E+00	5.63E-02	NaN	CD55, INS, ACTG2, ITGB6
GP6 Signaling Pathway	3.27E+00	3.73E-02	2.236	LAMB3, COL12A1, COL10A1, COL11A1, COL17A1
Clathrin-mediated Endocytosis Signaling	3.24E+00	2.90E-02	NaN	APOL1, MET, LYZ, INS, ACTG2, ITGB6
Inhibition of Matrix Metalloproteases	3.03E+00	7.69E-02	NaN	SDC1, MMP28, MMP11
IL-7 Signaling Pathway	2.97E+00	4.40E-02	2	MET, SLC2A1, IGHM, IGHG1
Tight Junction Signaling	2.84E+00	2.99E-02	NaN	CLDN1, MYLK, NECTIN1, ACTG2, MYH11
Glucocorticoid Receptor Signaling	2.79E+00	2.03E-02	NaN	KRT13, KRT17, KRT23, HSPA1A/HSPA1B, KRT6A, PTGS2, PLAU
p53 Signaling	2.65E+00	3.60E-02	NaN	CDKN2A, TP63, TRIM29, SFN
Agranulocyte Adhesion and Diapedesis	2.56E+00	2.59E-02	NaN	MMP28, CLDN1, MMP11, ACTG2, MYH11
HIF1Î± Signaling	2.47E+00	3.23E-02	NaN	MMP28, SLC2A1, EGLN3, MMP11
FXR/RXR Activation	2.45E+00	3.17E-02	NaN	APOL1, SDC1, INS, LPL
Atherosclerosis Signaling	2.44E+00	3.15E-02	NaN	APOL1, LYZ, LPL, COL10A1
Epithelial Adherens Junction Signaling	2.18E+00	2.67E-02	NaN	MET, NECTIN1, ACTG2, MYH11
Macropinocytosis Signaling	2.04E+00	3.45E-02	NaN	MET, INS, ITGB6
Renal Cell Carcinoma Signaling	2.02E+00	3.41E-02	NaN	MET, SLC2A1, EGLN3
Alanine Degradation III	2.01E+00	5.00E-01	NaN	GPT2
Alanine Biosynthesis II	2.01E+00	5.00E-01	NaN	GPT2
Cysteine Biosynthesis/Homocysteine Degradation	2.01E+00	5.00E-01	NaN	CBS/CBSL
Glutamine Degradation I	2.01E+00	5.00E-01	NaN	GLS2
Bladder Cancer Signaling	1.94E+00	3.19E-02	NaN	CDKN2A, MMP28, MMP11
Communication between Innate and Adaptive Immune Cells	1.93E+00	3.16E-02	NaN	IGHM, IGHG1, IGHD
Granulocyte Adhesion and Diapedesis	1.90E+00	2.21E-02	NaN	SDC1, MMP28, CLDN1, MMP11
ILK Signaling	1.78E+00	2.03E-02	NaN	ACTG2, MYH11, PTGS2, ITGB6
Retinol Biosynthesis	1.74E+00	4.76E-02	NaN	DHRS9, LPL
Proline Biosynthesis I	1.71E+00	2.50E-01	NaN	PYCR2
Virus Entry via Endocytic Pathways	1.70E+00	2.59E-02	NaN	CD55, ACTG2, ITGB6
Osteoarthritis Pathway	1.68E+00	1.89E-02	1	SPP1, H19, COL10A1, PTGS2
Leukocyte Extravasation Signaling	1.68E+00	1.90E-02	NaN	MMP28, CLDN1, MMP11, ACTG2
HGF Signaling	1.67E+00	2.52E-02	NaN	MET, CDKN2A, PTGS2
Integrin Signaling	1.63E+00	1.83E-02	0	MYLK, ACTG2, TNK2, ITGB6
Autoimmune Thyroid Disease Signaling	1.63E+00	4.17E-02	NaN	HLA-DQA1, IGHG1
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	1.60E+00	4.00E-02	NaN	CDKN2A, SFN
Cellular Effects of Sildenafil (Viagra)	1.56E+00	2.29E-02	NaN	MYLK, ACTG2, MYH11
Actin Cytoskeleton Signaling	1.54E+00	1.72E-02	NaN	INS, MYLK, ACTG2, MYH11
Proline Biosynthesis II (from Arginine)	1.53E+00	1.67E-01	NaN	PYCR2

Supplementary Table 3. Continued

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
Arginine Degradation VI (Arginase 2 Pathway)	1.53E+00	1.67E-01	NaN	PYCR2
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	1.41E+00	1.25E-01	NaN	KYNU
PXR/RXR Activation	1.39E+00	3.08E-02	NaN	SCD, INS
Prostanoid Biosynthesis	1.36E+00	1.11E-01	NaN	PTGS2
Citrulline Biosynthesis	1.36E+00	1.11E-01	NaN	GLS2
Remodeling of Epithelial Adherens Junctions	1.34E+00	2.90E-02	NaN	MET, ACTG2
Cdc42 Signaling	1.30E+00	1.80E-02	NaN	HLA-DQA1, MYLK, TNK2
Myc Mediated Apoptosis Signaling	1.26E+00	2.63E-02	NaN	CDKN2A, SFN
VDR/RXR Activation	1.24E+00	2.56E-02	NaN	SPP1, IGFBP3
Oleate Biosynthesis II (Animals)	1.20E+00	7.69E-02	NaN	SCD
Sertoli Cell-Sertoli Cell Junction Signaling	1.20E+00	1.63E-02	NaN	CLDN1, NECTIN1, ACTG2
Allograft Rejection Signaling	1.18E+00	2.35E-02	NaN	HLA-DQA1, IGHG1
Dendritic Cell Maturation	1.15E+00	1.55E-02	NaN	HLA-DQA1, COL10A1, IGHG1
B Cell Receptor Signaling	1.15E+00	1.55E-02	NaN	IGHM, IGHG1, IGHD
NAD biosynthesis II (from tryptophan)	1.14E+00	6.67E-02	NaN	KYNU
Superpathway of Citrulline Metabolism	1.14E+00	6.67E-02	NaN	GLS2
Regulation of Actin-based Motility by Rho	1.14E+00	2.22E-02	NaN	MYLK, ACTG2
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	1.14E+00	2.22E-02	NaN	SPP1, HLA-DQA1
IL-17 Signaling	1.13E+00	2.20E-02	NaN	CRP, PTGS2
Vitamin-C Transport	1.12E+00	6.25E-02	NaN	SLC2A1
Gap Junction Signaling	1.11E+00	1.49E-02	NaN	SP3, ACTG2, GJB2
DNA damage-induced 14-3-3Ïƒ Signaling	1.05E+00	5.26E-02	NaN	SFN
PPAR Signaling	1.05E+00	1.98E-02	NaN	INS, PTGS2
The Visual Cycle	1.03E+00	5.00E-02	NaN	DHRS9
Maturity Onset Diabetes of Young (MODY) Signaling	1.01E+00	4.76E-02	NaN	INS
VEGF Signaling	9.94E-01	1.83E-02	NaN	ACTG2, SFN
Fatty Acid Î±-oxidation	9.86E-01	4.55E-02	NaN	PTGS2
Type I Diabetes Mellitus Signaling	9.81E-01	1.80E-02	NaN	INS, HLA-DQA1
IGF-1 Signaling	9.74E-01	1.79E-02	NaN	IGFBP3, SFN
Systemic Lupus Erythematosus Signaling	9.64E-01	1.29E-02	NaN	IGL, IGHM, IGHG1
Cysteine Biosynthesis III (mammalia)	9.50E-01	4.17E-02	NaN	CBS/CBSL
Bupropion Degradation	9.33E-01	4.00E-02	NaN	CYP1B1
Tryptophan Degradation III (Eukaryotic)	9.33E-01	4.00E-02	NaN	KYNU
Paxillin Signaling	9.31E-01	1.68E-02	NaN	ACTG2, ITGB6
Pancreatic Adenocarcinoma Signaling	9.25E-01	1.67E-02	NaN	CDKN2A, PTGS2
Neuroprotective Role of THOP1 in Alzheimer's Disease	9.25E-01	1.67E-02	NaN	FAP, PRSS3
RhoA Signaling	9.02E-01	1.61E-02	NaN	MYLK, ACTG2
Signaling by Rho Family GTPases	8.89E-01	1.19E-02	NaN	MYLK, ACTG2, DES
Colorectal Cancer Metastasis Signaling	8.82E-01	1.18E-02	NaN	MMP28, MMP11, PTGS2
PI3K/AKT Signaling	8.63E-01	1.53E-02	NaN	PTGS2, SFN
Acetone Degradation I (to Methylglyoxal)	8.60E-01	3.33E-02	NaN	CYP1B1
Adipogenesis pathway	8.47E-01	1.49E-02	NaN	LPL, FABP4
G Protein Signaling Mediated by Tubby	8.34E-01	3.12E-02	NaN	INS

Supplementary Table 3. Continued

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
Aryl Hydrocarbon Receptor Signaling	8.12E-01	1.42E-02	NaN	CDKN2A, CYP1B1
DNA Methylation and Transcriptional Repression Signaling	8.09E-01	2.94E-02	NaN	HIST1H4L
Inhibition of Angiogenesis by TSP1	8.09E-01	2.94E-02	NaN	SDC1
Retinoate Biosynthesis I	8.09E-01	2.94E-02	NaN	DHRS9
Coagulation System	7.98E-01	2.86E-02	NaN	PLAU
MIF-mediated Glucocorticoid Regulation	7.98E-01	2.86E-02	NaN	PTGS2
IL-12 Signaling and Production in Macrophages	7.88E-01	1.37E-02	NaN	APOL1, LYZ
Ethanol Degradation II	7.76E-01	2.70E-02	NaN	DHRS9
Superpathway of Methionine Degradation	7.76E-01	2.70E-02	NaN	CBS/CBSL
Complement System	7.76E-01	2.70E-02	NaN	CD55
Ovarian Cancer Signaling	7.70E-01	1.33E-02	NaN	CDKN2A, PTGS2
Antigen Presentation Pathway	7.65E-01	2.63E-02	NaN	HLA-DQA1
Oncostatin M Signaling	7.45E-01	2.50E-02	NaN	PLAU
Noradrenaline and Adrenaline Degradation	7.45E-01	2.50E-02	NaN	DHRS9
Mechanisms of Viral Exit from Host Cells	7.35E-01	2.44E-02	NaN	ACTG2
Estrogen Biosynthesis	7.35E-01	2.44E-02	NaN	CYP1B1
Hepatic Cholestasis	7.27E-01	1.25E-02	NaN	INS, GCG
Intrinsic Prothrombin Activation Pathway	7.26E-01	2.38E-02	NaN	COL10A1
MIF Regulation of Innate Immunity	7.17E-01	2.33E-02	NaN	PTGS2
Role of p14/p19ARF in Tumor Suppression	7.17E-01	2.33E-02	NaN	CDKN2A
Neuroinflammation Signaling Pathway	7.00E-01	9.65E-03	NaN	CRP, HLA-DQA1, PTGS2
Aldosterone Signaling in Epithelial Cells	6.95E-01	1.19E-02	NaN	HSPA1A/HSPA1B, DNAJB1
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	6.90E-01	2.17E-02	NaN	SPP1
Graft-versus-Host Disease Signaling	6.74E-01	2.08E-02	NaN	HLA-DQA1
Acute Phase Response Signaling	6.65E-01	1.14E-02	NaN	CRP, CP
Semaphorin Signaling in Neurons	6.36E-01	1.89E-02	NaN	MET
PPARÎ±/RXRÎ± Activation	6.30E-01	1.08E-02	NaN	INS, LPL
Transcriptional Regulatory Network in Embryonic Stem Cells	6.29E-01	1.85E-02	NaN	HIST1H4L
Triacylglycerol Degradation	6.29E-01	1.85E-02	NaN	LPL
Cancer Drug Resistance By Drug Efflux	6.22E-01	1.82E-02	NaN	PTGS2
RAR Activation	6.17E-01	1.05E-02	NaN	DHRS9, IGFBP3
Nicotine Degradation III	6.15E-01	1.79E-02	NaN	CYP1B1
Unfolded protein response	6.15E-01	1.79E-02	NaN	HSPA1A/HSPA1B
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	6.04E-01	1.03E-02	NaN	APOL1, LYZ
Nur77 Signaling in T Lymphocytes	5.96E-01	1.69E-02	NaN	HLA-DQA1
NRF2-mediated Oxidative Stress Response	5.88E-01	1.01E-02	NaN	ACTG2, DNAJB1
Adrenomedullin Signaling Pathway	5.85E-01	1.00E-02	NaN	ADM, MYLK
Melanoma Signaling	5.83E-01	1.64E-02	NaN	CDKN2A
3-phosphoinositide Biosynthesis	5.82E-01	9.95E-03	NaN	MET, CILP
Calcium Signaling	5.67E-01	9.71E-03	NaN	TP63, MYH11
Melatonin Degradation I	5.60E-01	1.54E-02	NaN	CYP1B1
Nicotine Degradation II	5.60E-01	1.54E-02	NaN	CYP1B1
Calcium-induced T Lymphocyte Apoptosis	5.54E-01	1.52E-02	NaN	HLA-DQA1

Supplementary Table 3. Continued

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
Cell Cycle: G1/S Checkpoint Regulation	5.48E-01	1.49E-02	NaN	CDKN2A
Eicosanoid Signaling	5.48E-01	1.49E-02	NaN	PTGS2
AMPK Signaling	5.39E-01	9.26E-03	NaN	SLC2A1, INS
Role of IL-17A in Arthritis	5.38E-01	1.45E-02	NaN	PTGS2
Superpathway of Melatonin Degradation	5.32E-01	1.43E-02	NaN	CYP1B1
ERK5 Signaling	5.22E-01	1.39E-02	NaN	SFN
MSP-RON Signaling Pathway	5.22E-01	1.39E-02	NaN	ACTG2
T Helper Cell Differentiation	5.17E-01	1.37E-02	NaN	HLA-DQA1
GPCR-Mediated Integration of Enteroendocrine Signaling Exemplified by an L Cell	5.17E-01	1.37E-02	NaN	GCG
EIF2 Signaling	5.10E-01	8.81E-03	NaN	INS, ACTG2
Agrin Interactions at Neuromuscular Junction	5.08E-01	1.33E-02	NaN	ACTG2
Glioma Invasiveness Signaling	5.03E-01	1.32E-02	NaN	PLAU
Serotonin Degradation	4.98E-01	1.30E-02	NaN	DHRS9
Protein Kinase A Signaling	4.97E-01	7.48E-03	NaN	MYLK, PTGS2, SFN
Role of MAPK Signaling in the Pathogenesis of Influenza	4.94E-01	1.28E-02	NaN	PTGS2
CD40 Signaling	4.89E-01	1.27E-02	NaN	PTGS2
Superpathway of Inositol Phosphate Compounds	4.87E-01	8.47E-03	NaN	MET, CILP
Cyclins and Cell Cycle Regulation	4.80E-01	1.23E-02	NaN	CDKN2A
Non-Small Cell Lung Cancer Signaling	4.72E-01	1.20E-02	NaN	CDKN2A
Growth Hormone Signaling	4.63E-01	1.18E-02	NaN	IGFBP3
Small Cell Lung Cancer Signaling	4.63E-01	1.18E-02	NaN	PTGS2
Leptin Signaling in Obesity	4.59E-01	1.16E-02	NaN	INS
HIPPO signaling	4.55E-01	1.15E-02	NaN	SFN
Huntington's Disease Signaling	4.55E-01	8.00E-03	NaN	HSPA1A/HSPA1B, DNAJB1
Crosstalk between Dendritic Cells and Natural Killer Cells	4.47E-01	1.12E-02	NaN	ACTG2
OX40 Signaling Pathway	4.39E-01	1.10E-02	NaN	HLA-DQA1
FGF Signaling	4.39E-01	1.10E-02	NaN	MET
FcÎ^{3} Receptor-mediated Phagocytosis in Macrophages and Monocytes	4.32E-01	1.08E-02	NaN	ACTG2
Death Receptor Signaling	4.32E-01	1.08E-02	NaN	ACTG2
TGF-Î^{2} Signaling	4.32E-01	1.08E-02	NaN	INHBA
HER-2 Signaling in Breast Cancer	4.28E-01	1.06E-02	NaN	ITGB6
IL-4 Signaling	4.25E-01	1.05E-02	NaN	HLA-DQA1
Protein Ubiquitination Pathway	4.23E-01	7.55E-03	NaN	HSPA1A/HSPA1B, DNAJB1
Sumoylation Pathway	4.21E-01	1.04E-02	NaN	SP3
TR/RXR Activation	4.14E-01	1.02E-02	NaN	SLC2A1
FAK Signaling	3.91E-01	9.52E-03	NaN	ACTG2
Cholecystokinin/Gastrin-mediated Signaling	3.85E-01	9.35E-03	NaN	PTGS2
PAK Signaling	3.85E-01	9.35E-03	NaN	MYLK
Antioxidant Action of Vitamin C	3.82E-01	9.26E-03	NaN	SLC2A1

Supplementary Table 3. Continued

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
Chronic Myeloid Leukemia Signaling	3.70E-01	8.93E-03	NaN	CDKN2A
GPCR-Mediated Nutrient Sensing in Enteroendocrine Cells	3.70E-01	8.93E-03	NaN	GCG
Glioma Signaling	3.48E-01	8.33E-03	NaN	CDKN2A
G Beta Gamma Signaling	3.48E-01	8.33E-03	NaN	CAV2
iCOS-iCOSL Signaling in T Helper Cells	3.40E-01	8.13E-03	NaN	HLA-DQA1
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	3.27E-01	6.25E-03	NaN	IGHG1, PRSS3
Phagosome Formation	3.20E-01	7.63E-03	NaN	IGHG1
CD28 Signaling in T Helper Cells	3.18E-01	7.58E-03	NaN	HLA-DQA1
IL-6 Signaling	3.13E-01	7.46E-03	NaN	CRP
Th1 Pathway	3.11E-01	7.41E-03	NaN	HLA-DQA1
CCR3 Signaling in Eosinophils	3.09E-01	7.35E-03	NaN	MYLK
14-3-3-mediated Signaling	3.06E-01	7.30E-03	NaN	SFN
Androgen Signaling	3.06E-01	7.30E-03	NaN	DNAJB1
Iron homeostasis signaling pathway	3.06E-01	7.30E-03	NaN	CP
p70S6K Signaling	3.04E-01	7.25E-03	NaN	SFN
Corticotropin Releasing Hormone Signaling	3.02E-01	7.19E-03	NaN	PTGS2
Human Embryonic Stem Cell Pluripotency	2.93E-01	6.99E-03	NaN	INHBA
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	2.91E-01	6.94E-03	NaN	CILP
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	2.91E-01	6.94E-03	NaN	CILP
Insulin Receptor Signaling	2.85E-01	6.80E-03	NaN	INS
Hereditary Breast Cancer Signaling	2.79E-01	6.67E-03	NaN	SFN
Th2 Pathway	2.79E-01	6.67E-03	NaN	HLA-DQA1
Type II Diabetes Mellitus Signaling	2.72E-01	6.49E-03	NaN	INS
3-phosphoinositide Degradation	2.64E-01	6.33E-03	NaN	CILP
D-myo-inositol-5-phosphate Metabolism	2.57E-01	6.17E-03	NaN	CILP
PKCÎ¸ Signaling in T Lymphocytes	2.52E-01	6.06E-03	NaN	HLA-DQA1
Glioblastoma Multiforme Signaling	2.47E-01	5.95E-03	NaN	CDKN2A
Tec Kinase Signaling	2.44E-01	5.88E-03	NaN	ACTG2
eNOS Signaling	2.40E-01	5.81E-03	NaN	HSPA1A/HSPA1B
Wnt/Î²-catenin Signaling	2.40E-01	5.81E-03	NaN	CDKN2A
RhoGDI Signaling	2.33E-01	5.65E-03	NaN	ACTG2
Germ Cell-Sertoli Cell Junction Signaling	2.29E-01	5.59E-03	NaN	ACTG2
Th1 and Th2 Activation Pathway	2.21E-01	5.41E-03	NaN	HLA-DQA1
NF-ÎºB Signaling	2.18E-01	5.35E-03	NaN	INS
Role of NFAT in Regulation of the Immune Response	2.11E-01	5.21E-03	NaN	HLA-DQA1
Regulation of the Epithelial-Mesenchymal Transition Pathway	2.07E-01	5.13E-03	NaN	MET
Endothelin-1 Signaling	2.06E-01	5.10E-03	NaN	PTGS2
IL-8 Signaling	0.00E+00	4.93E-03	NaN	PTGS2
mTOR Signaling	0.00E+00	4.83E-03	NaN	INS
Thrombin Signaling	0.00E+00	4.76E-03	NaN	MYLK
LPS/IL-1 Mediated Inhibition of RXR Function	0.00E+00	4.50E-03	NaN	FABP4
Axonal Guidance Signaling	0.00E+00	4.38E-03	NaN	MET, MMP11

Supplementary Table 3. Continued

Canonical pathways	–log(p-value)	Ratio	z-score	Molecules
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	0.00E+00	4.29E-03	NaN	SPP1
Phospholipase C Signaling	0.00E+00	4.10E-03	NaN	IGHG1
Sirtuin Signaling Pathway	0.00E+00	3.42E-03	NaN	SLC2A1
Xenobiotic Metabolism Signaling	0.00E+00	3.38E-03	NaN	CYP1B1
Molecular Mechanisms of Cancer	0.00E+00	2.54E-03	NaN	CDKN2A

MTV, metabolic tumor volume.

Supplementary Table 4. Upstream Analysis in MTV$_{2.5}$ High Tumor Samples

Upstream regulator	Molecule type	Predicted activation state	Activation z-score	p-value
IFNG	cytokine	Activated	3.657	1.04E-12
FGF2	growth factor	Activated	3.221	2.25E-06
JUN	transcription regulator	Activated	3.212	3.55E-07
lipopolysaccharide	chemical drug	Activated	3.186	1.26E-10
TNF	cytokine	Activated	3.079	1.55E-12
HGF	growth factor	Activated	2.903	1.79E-04
IL1B	cytokine	Activated	2.794	6.13E-12
RELA	transcription regulator	Activated	2.754	4.82E-05
Cg	complex	Activated	2.638	2.12E-07
IL5	cytokine	Activated	2.611	4.76E-04
Insulin	group	Activated	2.547	2.83E-03
SP1	transcription regulator	Activated	2.49	1.01E-07
tretinoin	chemical - endogenous mammalian	Activated	2.474	1.57E-06
PPARG	ligand-dependent nuclear receptor	Activated	2.454	1.04E-08
STAT1	transcription regulator	Activated	2.449	1.68E-03
ARNT2	transcription regulator	Activated	2.449	5.54E-04
OSM	cytokine	Activated	2.433	1.62E-02
FOS	transcription regulator	Activated	2.429	3.56E-04
Akt	group	Activated	2.42	4.66E-04
mycophenolic acid	chemical drug	Activated	2.412	3.86E-06
tributyrin	chemical drug	Activated	2.407	7.90E-07
AGT	growth factor	Activated	2.402	2.11E-06
BMP4	growth factor	Activated	2.383	5.03E-05
Tgf beta	group	Activated	2.364	3.73E-07
bucladesine	chemical toxicant	Activated	2.315	9.49E-04
EGFR	kinase	Activated	2.26	2.72E-05
EGF	growth factor	Activated	2.255	7.75E-06
SIM1	transcription regulator	Activated	2.236	3.95E-03
FN1	enzyme	Activated	2.219	3.64E-03
PRL	cytokine	Activated	2.213	2.29E-03
NFkB (complex)	complex	Activated	2.208	2.80E-04
cis-urocanic acid	chemical drug	Activated	2.207	6.37E-08
alitretinoin	chemical drug	Activated	2.207	1.17E-04
BMP2	growth factor	Activated	2.2	3.28E-03
CD40LG	cytokine	Activated	2.187	7.26E-04
3,4,5,3',4'-pentachlorobiphenyl	chemical toxicant	Activated	2.186	4.93E-05
SREBF1	transcription regulator	Activated	2.178	2.47E-04
MYD88	other	Activated	2.168	9.93E-03
Vegf	group	Activated	2.164	7.30E-06
PDGF BB	complex	Activated	2.162	5.71E-07
EDN1	cytokine	Activated	2.162	2.95E-03
NFKB1	transcription regulator	Activated	2.161	2.25E-03
SMARCB1	transcription regulator	Activated	2.157	1.56E-03
CTNNB1	transcription regulator	Activated	2.062	3.46E-08
CEBPB	transcription regulator	Activated	2.042	1.38E-07
TGFB1	growth factor	Activated	2.038	1.41E-15
IRS2	enzyme	Activated	2	4.82E-05
HBEGF	growth factor	Activated	2	5.83E-05

MTV, metabolic tumor volume.

Supplementary Table 5. Predicted Diseases and Functions in $MTV_{2.5}$ High Tumor Samples

Diseases or functions annotation	p-value	Predicted activation state	Activation z-score
Invasion of tumor	1.36E-05	Increased	2.007
Cell spreading	7.85E-05	Increased	2.017
Proliferation of tumor cells	7.14E-05	Increased	2.033
Genital tumor	5.47E-06	Increased	2.039
Quantity of carbohydrate	1.99E-05	Increased	2.042
Migration of tumor cells	1.30E-06	Increased	2.066
Activation of antigen presenting cells	4.04E-05	Increased	2.158
Cell movement of pancreatic cancer cell lines	2.70E-05	Increased	2.2
Metabolism of nucleotide	9.56E-05	Increased	2.225
Metabolism of nucleic acid component or derivative	1.17E-04	Increased	2.225
Survival of organism	3.33E-07	Increased	2.275
Binding of DNA	4.77E-05	Increased	2.355
Invasion of tumor cell lines	8.94E-08	Increased	2.387
Cell viability	2.44E-07	Increased	2.402
Invasion of tumor cells	7.67E-05	Increased	2.414
Metabolism of carbohydrate	1.94E-05	Increased	2.628
Organismal death	1.20E-06	Decreased	-3.967
Morbidity or mortality	1.94E-07	Decreased	-3.899
Necrosis	5.32E-10	Decreased	-3.65
Cell death	7.02E-08	Decreased	-3.081
Inflammation of absolute anatomical region	2.62E-08	Decreased	-2.906
Apoptosis	1.99E-05	Decreased	-2.763
Cell death of tumor cell lines	7.71E-08	Decreased	-2.495
Inflammation of organ	5.50E-11	Decreased	-2.328
Apoptosis of tumor cell lines	2.42E-07	Decreased	-2.265
Glomerulosclerosis	2.95E-05	Decreased	-2.178
Contraction of muscle cells	8.39E-06	Decreased	-2.172
Inflammation of body cavity	1.45E-07	Decreased	-2.115

MTV, metabolic tumor volume.

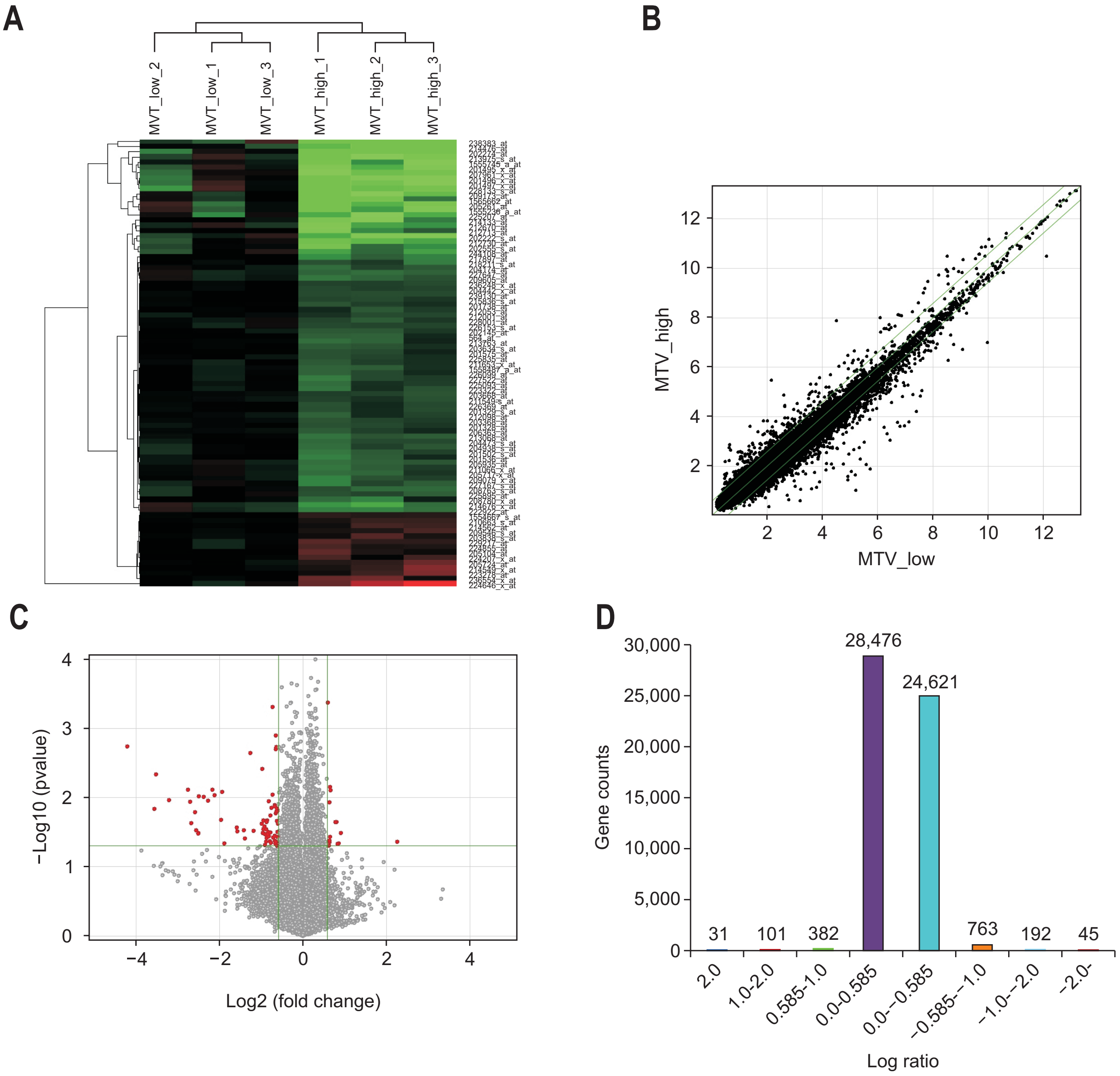
Supplementary Table 6. Predicted Regulator Effects in $MTV_{2.5}$ High Tumor Samples

ID	Consistency score	Regulators	Diseases & functions	Known regulator-disease/ function relationship
1	7.071	FOS, MYD88, U0126	Invasion of tumor cells, Proliferation of tumor cells	50% (3/6)
2	6.641	FOS, IL1B, U0126	Invasion of tumor cells, Proliferation of tumor cells	67% (4/6)
3	6.641	IL1B, MYD88, U0126	Invasion of tumor, Proliferation of tumor cells	50% (3/6)
4	6.364	CD40LG, MYD88, U0126	Invasion of tumor, Proliferation of tumor cells	50% (3/6)
5	6.364	EDN1, MYD88, U0126	Invasion of tumor, Proliferation of tumor cells	67% (4/6)
6	6.364	actinomycin D, FOS, U0126	Invasion of tumor cells, Proliferation of tumor cells	67% (4/6)
7	6.01	cycloheximide, FOS, U0126	Invasion of tumor cells, Proliferation of tumor cells	67% (4/6)
8	6.008	CD40LG, IL1B, U0126	Invasion of tumor, Proliferation of tumor cells	67% (4/6)
9	5.692	IL1B, NFKB1, U0126	Invasion of tumor, Proliferation of tumor cells	50% (3/6)
10	5.5	AGT, Tgf beta, U0126	Invasion of tumor cells	33% (1/3)
11	5.5	HGF, Tgf beta, U0126	Invasion of tumor cells	67% (2/3)
12	5.5	PDGF BB, Tgf beta, U0126	Invasion of tumor cells	33% (1/3)
13	5.5	SB203580, Tgf beta, U0126	Invasion of tumor cells	33% (1/3)
14	5.5	Tgf beta, tretinoin, U0126	Invasion of tumor cells	67% (2/3)
15	5.307	EGFR, PD98059, TGFB1	Invasion of tumor cells	100% (3/3)
16	5.307	EGFR, TGFB1, TNF	Invasion of tumor cells	67% (2/3)
17	5.307	PD98059, TGFB1, TNF	Invasion of tumor cells	67% (2/3)
18	5.307	Tgf beta, TGFB1, U0126	Invasion of tumor cells	67% (2/3)
19	5	BMP2, Tgf beta, U0126	Invasion of tumor cells	67% (2/3)
20	5	RELA, Tgf beta, U0126	Invasion of tumor cells	33% (1/3)
21	5	Tgf beta, U0126, Vegf	Invasion of tumor cells	67% (2/3)
22	4.899	EGF, EGFR, TGFB1	Invasion of tumor cells	100% (3/3)
23	4.899	EGF, PD98059, TGFB1	Invasion of tumor cells	100% (3/3)
24	4.899	EGF, TGFB1, TNF	Invasion of tumor cells	67% (2/3)
25	4.899	EGFR, FGF2, TGFB1	Invasion of tumor cells	67% (2/3)
26	4.899	EGFR, FOS, TGFB1	Invasion of tumor cells	67% (2/3)
27	4.899	EGFR, JUN, TGFB1	Invasion of tumor cells	67% (2/3)
28	4.899	EGFR, TGFB1, tyrphostin AG 1478	Invasion of tumor cells	100% (3/3)
29	4.899	FGF2, PD98059, TGFB1	Invasion of tumor cells	67% (2/3)
30	4.899	FGF2, TGFB1, TNF	Invasion of tumor cells	33% (1/3)
31	4.899	FOS, PD98059, TGFB1	Invasion of tumor cells	67% (2/3)
32	4.899	FOS, TGFB1, TNF	Invasion of tumor cells	33% (1/3)
33	4.899	JUN, PD98059, TGFB1	Invasion of tumor cells	67% (2/3)
34	4.899	JUN, TGFB1, TNF	Invasion of tumor cells	33% (1/3)
35	4.899	PD98059, TGFB1, tyrphostin AG 1478	Invasion of tumor cells	100% (3/3)
36	4.899	TGFB1, TNF, tyrphostin AG 1478	Invasion of tumor cells	67% (2/3)
37	4.491	Cg, EGFR, TGFB1	Invasion of tumor cells	67% (2/3)
38	4.491	Cg, PD98059, TGFB1	Invasion of tumor cells	67% (2/3)
39	4.491	Cg, TGFB1, TNF	Invasion of tumor cells	33% (1/3)
40	4.491	EDN1, EGFR, TGFB1	Invasion of tumor cells	100% (3/3)
41	4.491	EDN1, PD98059, TGFB1	Invasion of tumor cells	100% (3/3)
42	4.491	EDN1, TGFB1, TNF	Invasion of tumor cells	67% (2/3)
43	4.491	EGFR, GATA4, TGFB1	Invasion of tumor cells	67% (2/3)

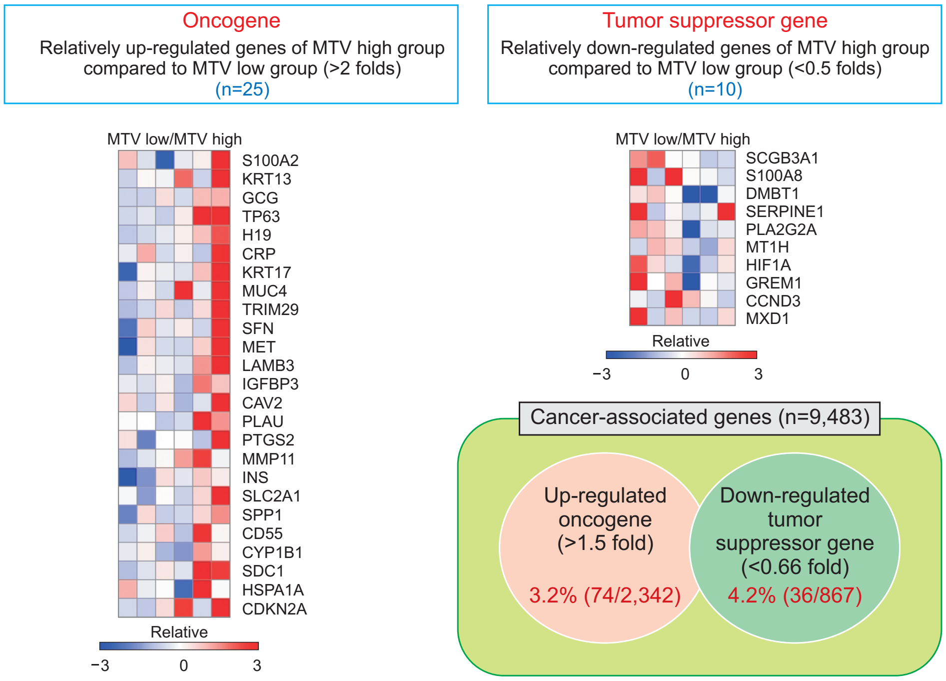
Supplementary Table 6. Continued

ID	Consistency score	Regulators	Diseases & functions	Known regulator-disease/ function relationship
44	4.491	GATA4, PD98059, TGFB1	Invasion of tumor cells	67% (2/3)
45	4.491	GATA4, TGFB1, TNF	Invasion of tumor cells	33% (1/3)
46	4.359	SP1, Tgf beta, U0126	Genital tumor, Invasion of tumor cells	17% (1/6)
47	4.264	LY294002, Tgf beta, U0126	Genital tumor, Invasion of tumor cells	50% (3/6)
48	4.082	EGFR, FN1, TGFB1	Invasion of tumor cells	100% (3/3)
49	4.082	FN1, PD98059, TGFB1	Invasion of tumor cells	100% (3/3)
50	4.082	FN1, TGFB1, TNF	Invasion of tumor cells	67% (2/3)
51	0	SREBF1	Proliferation of tumor cells	100% (1/1)
52	-3	lipopolysaccharide	Proliferation of tumor cells	100% (1/1)
53	-3.78	IFNG	Proliferation of tumor cells	100% (1/1)
54	-4.899	CTNNB1	Proliferation of tumor cells	100% (1/1)
55	-7.506	cis-urocanic acid	Proliferation of tumor cells	0% (0/1)
56	-8.083	OSM	Proliferation of tumor cells	100% (1/1)
57	-8.083	PRL	Proliferation of tumor cells	100% (1/1)
58	-8.083	bucladesine	Proliferation of tumor cells	0% (0/1)

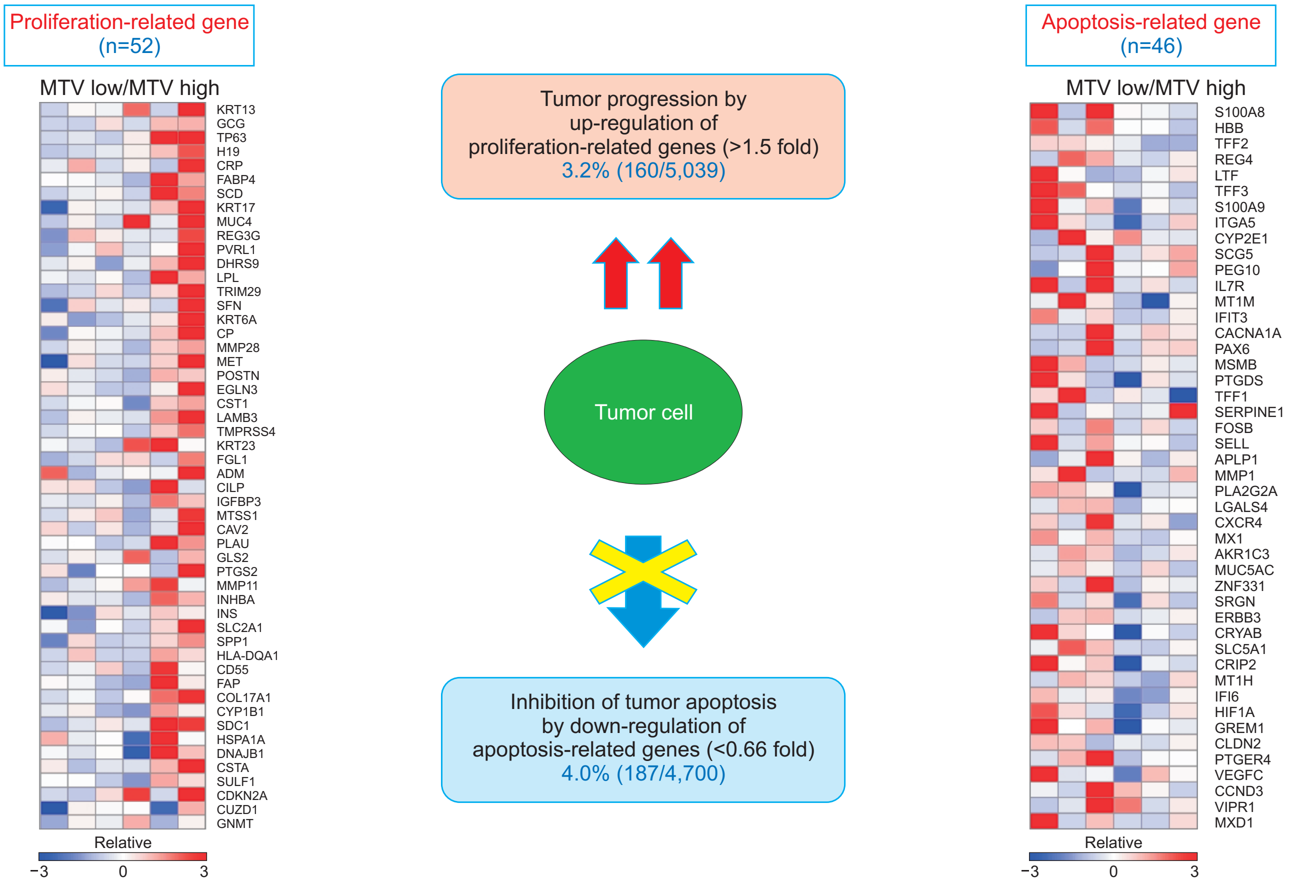
MTV, metabolic tumor volume.



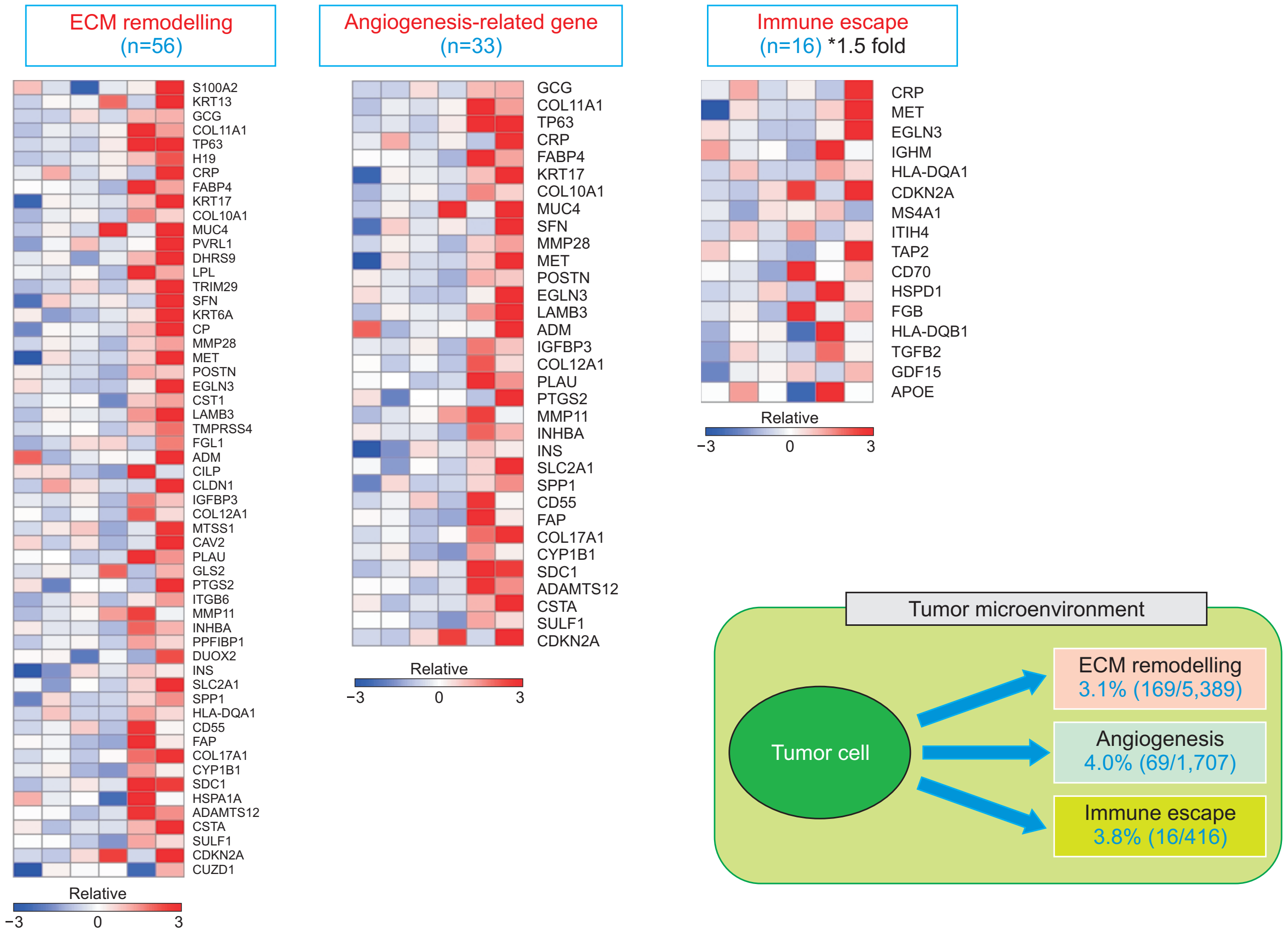
Supplementary Fig. 1. Differentially expressed genes according to metabolic phenotype (metabolic tumor volume [MTV] high; $MTV_{2.5}$ ≥4.5 vs MTV low; $MTV_{2.5}$ <4.5). (A) Heatmap of significant genes for MTV high and low groups. (B) Scatter plot for gene expression patterns in MTV high and low groups. (C) Volcano plot for significantly upregulated (fold change [FC] >2) and downregulated (FC <2) genes according to metabolic phenotype. (D) Distribution of fold changes in the relative expression of the MTV high group versus the MTV low group.



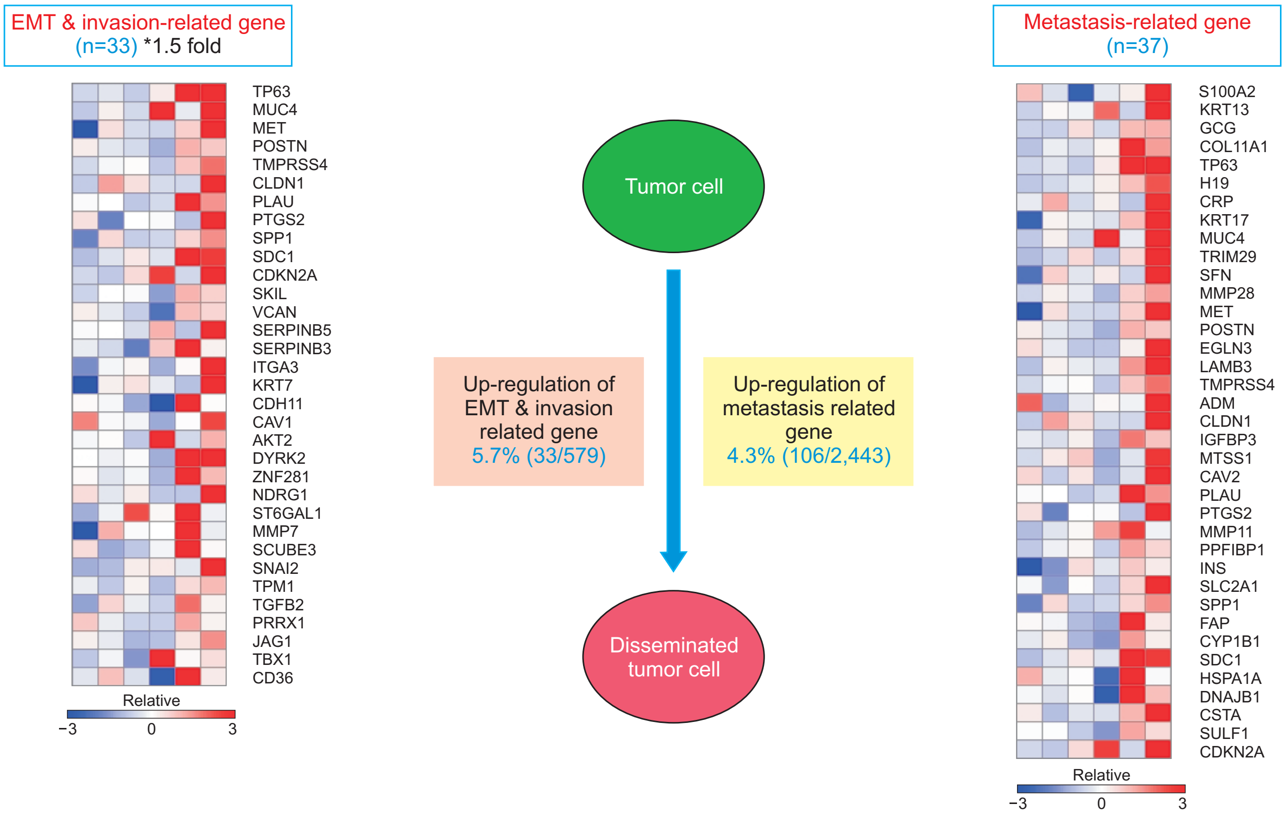
Supplementary Fig. 2. Relative gene expression between MTV high versus low–oncogene & tumor suppressor genes. MTV, metabolic tumor volume.



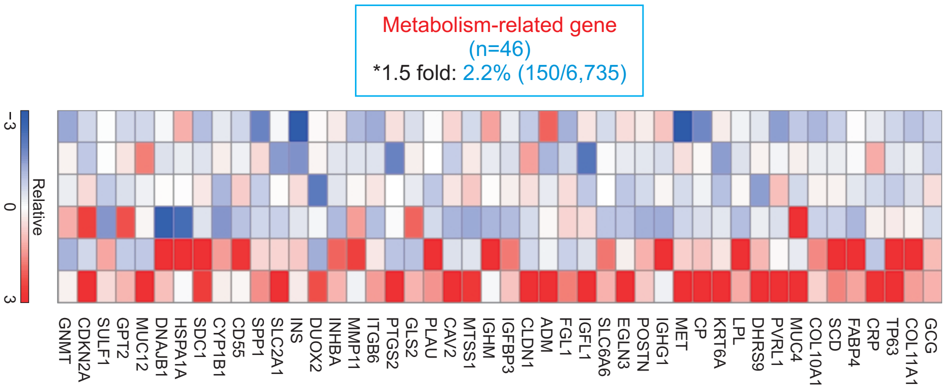
Supplementary Fig. 3. Relative gene expression between MTV high versus low–proliferation & apoptosis related genes. MTV, metabolic tumor volume.



Supplementary Fig. 4. Relative gene expression between MTV high versus low–ECM & angiogenesis & immune escape-related genes.



Supplementary Fig. 5. Relative gene expression between MTV high versus low– EMT & invasion & metastasis related genes. MTV, metabolic tumor volume.



Supplementary Fig. 6. Relative gene expression between MTV high versus low–metabolism-related genes.
MTV, metabolic tumor volume.