

Supplementary Material

1. Supplementary Results

1.1. Identification of consistent prognostic markers across TCGA-LIHC and ScRNA-Meta cohorts

In the TCGA-LIHC and ScRNA-Meta cohorts, 500 upregulated genes and 15 downregulated genes were identified as the overlapping genes (Fig. S1A-B). Among these 515 genes, 53 were consistently identified as prognostic markers in both the TCGA-LIHC and GSE14520 cohorts, highlighting their potential as reliable prognostic features (Fig. S1C).

1.2. Prognostic significance and expression patterns of PCD-Metabolism model genes

In the PCD-Metabolism model genes, HDAC2, MARCKS, and SPP1 were the top three contributors to the risk model (Fig. S2A). All genes, except LDHA, were significantly upregulated in tumors compared to normal tissues ($P < 0.05$, Fig. S2B). HSP90B1 was not associated with HCC prognosis, while the remaining genes exhibited a positive correlation with prognosis ($P < 0.05$, Fig. S2C). We further evaluated the expression and prognostic significance of these genes in ten other cancer types. As shown in Fig. S2B, most of these genes were upregulated in cancers such as BRCA and CHOL. However, their prognostic value in terms of OS and DSS was comparatively lower in these cancers than in HCC (Fig. S2C-D), emphasizing the cancer-type specificity of these genes and their unique prognostic relevance in HCC.

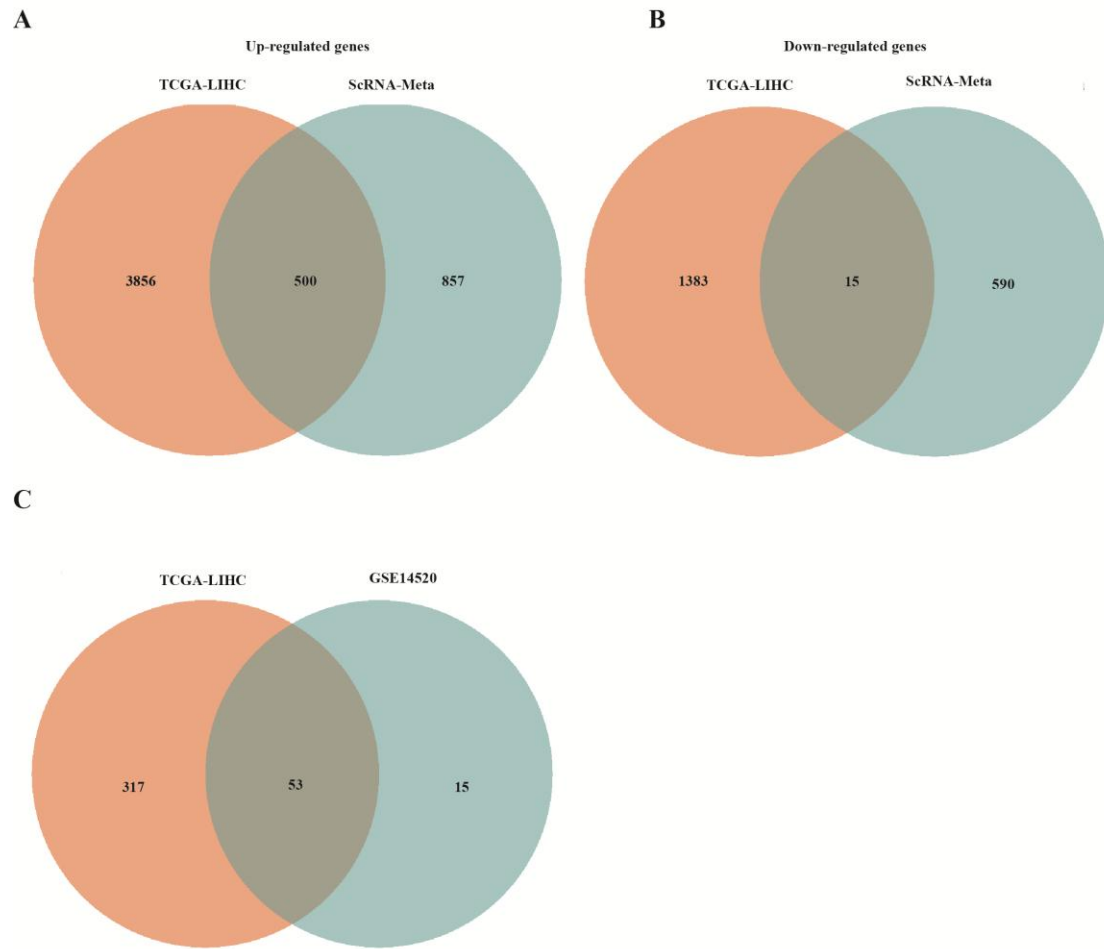


Fig. S1. PCD-Metabolism crosstalk features identified across both single-cell and bulk transcriptomes. (A) Intersection of upregulated genes identified as PCD-metabolism crosstalk features in both single-cell and bulk transcriptomes. (B) Intersection of downregulated genes identified as PCD-metabolism crosstalk features in both single-cell and bulk transcriptomes. (C) Prognostic signatures significantly associated with patient outcomes in both the TCGA-LIHC and GSE14520 cohorts.

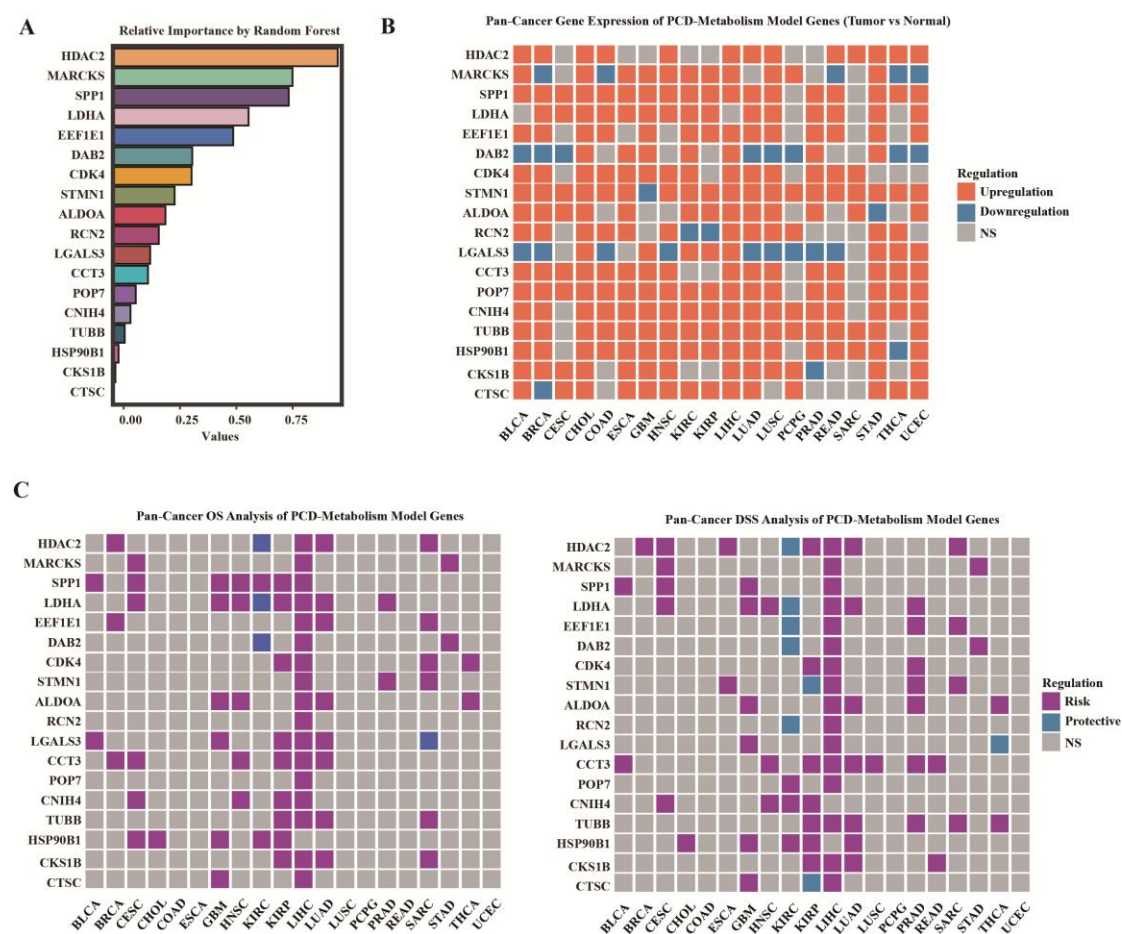


Fig. S2. Importance ranking of PCD-metabolism model genes in the StepCox+RSF model and pan-cancer analysis of model genes. (A) Importance ranking of 18 key PCD-metabolism genes in the StepCox+RSF risk model. The bar chart shows the importance scores of each gene. (B) Pan-cancer analysis of gene expression between tumor and normal tissues using the model genes. (C) Pan-cancer analysis of overall survival (OS) and disease-specific survival (DSS) using the model genes.

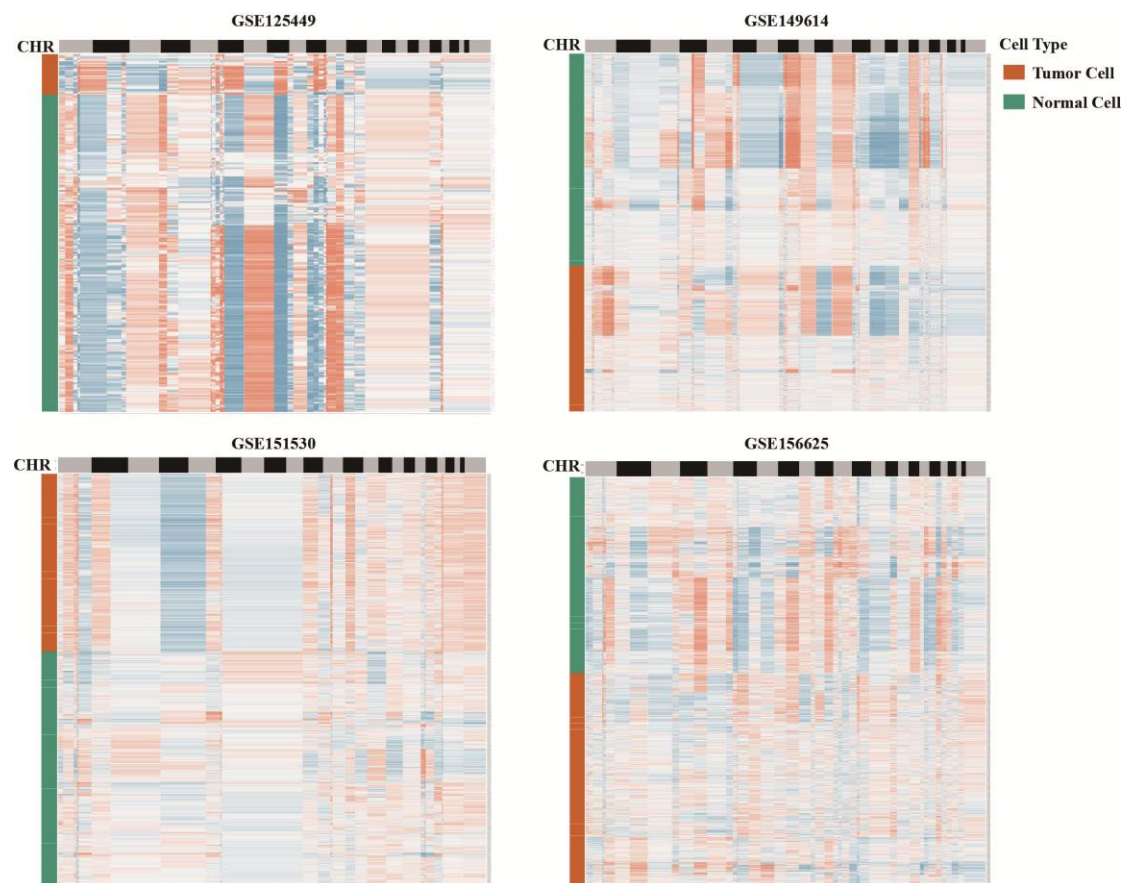


Fig. S4 Malignancy assessment of hepatocytes across all datasets of the scRNA-seq cohort.

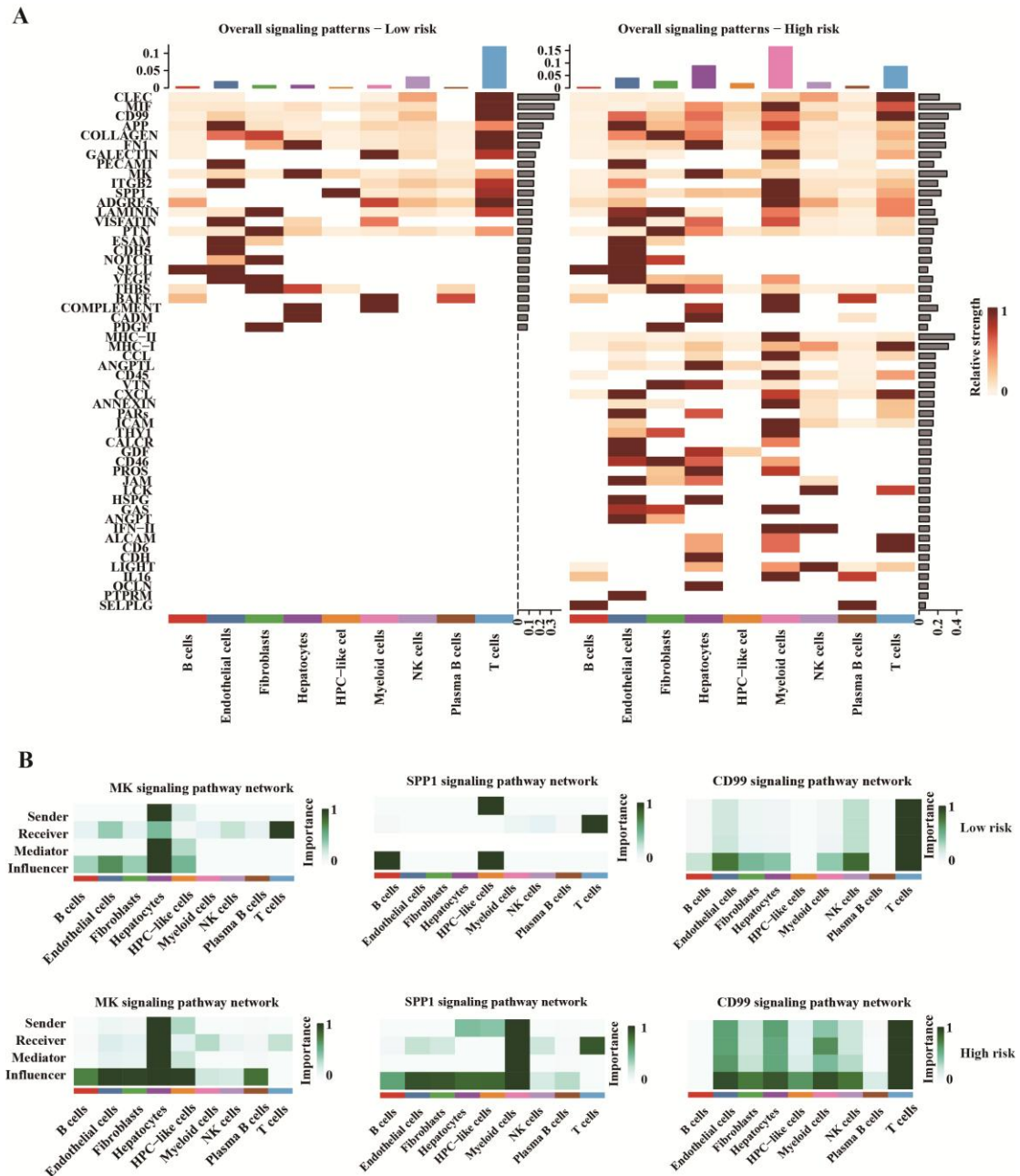


Fig. S5. Signaling patterns of intercellular communication in low- and high-PCD-Metabolism groups. (A) Heatmap showing the overall signal flow (both outgoing and incoming) of each cell population. (B) MK, SPP1, and CD99 signaling pathway interactions in low- and high-PCD-Metabolism groups.

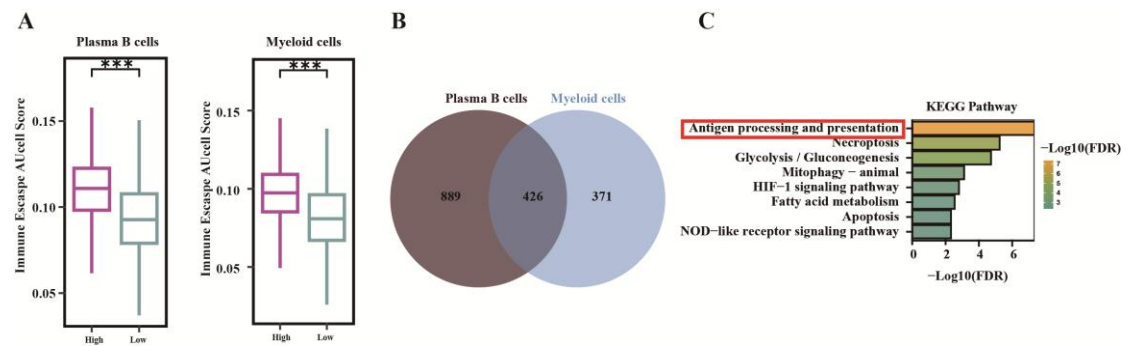


Fig. S6. Immune evasion and differential gene expression analysis between high and low risk subgroups in myeloid and plasma cells. (A) Immune evasion scores in plasma cells and myeloid cells between high and low PCD-Metabolism risk subgroups. (B) Differential expression analysis identifying genes with significant expression differences between high and low PCD-Metabolism risk groups in myeloid cells and plasma cells, revealing 426 overlapping genes. (C) KEGG enrichment analysis of overlapping genes between myeloid cells and plasma cells.

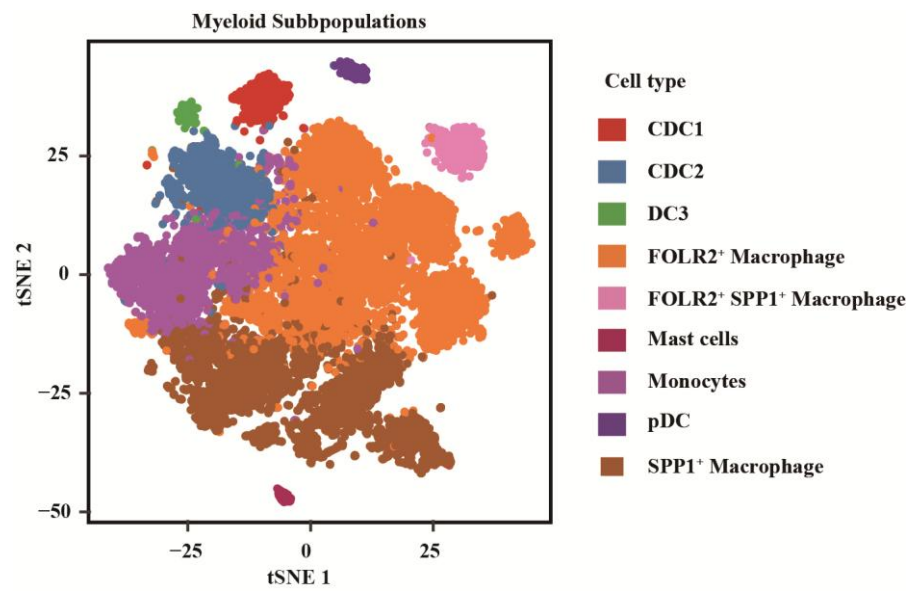


Fig. S7. t-SNE analysis of myeloid cell subpopulations.

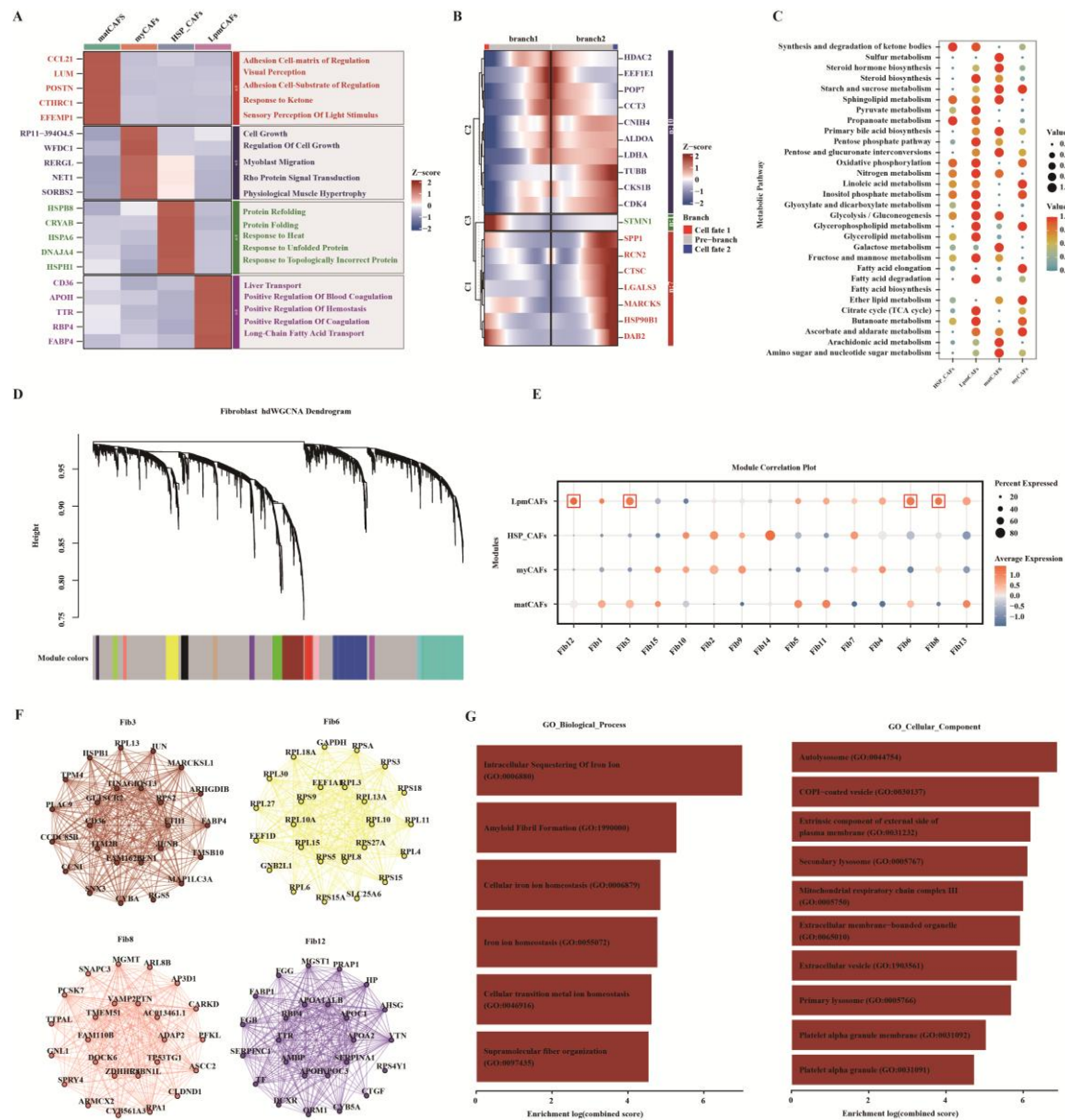


Fig. S8. Analysis of fibroblast subtypes and PCD-Metabolism regulation. (A) Heatmap showing the top 5 DEGs for each fibroblast subtype. (B) Dynamic regulation of PCD-Metabolism model genes during the differentiation period. (C) Comparison of metabolic activity across four fibroblast subtypes. (D) hdWGCNA analysis with dynamic network tree cutting, identifying 13 modules. (E) Scatter plots depicting the association between modules and distinct fibrotic subtypes, with higher percentage and average expression indicating stronger module associations. (F) Top 25 hub genes identified in hdWGCNA modules 3, 6, 8, and 12. (G) GO enrichment analysis of Module 3.

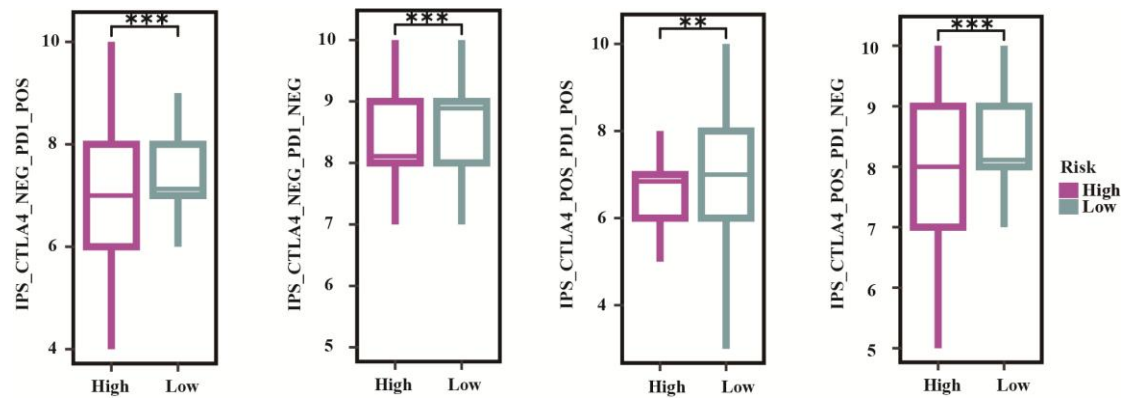


Fig. S9. Comparison of IPS scores between high and low PCD-Metabolism risk subgroups in the TCGA-LIHC cohort.

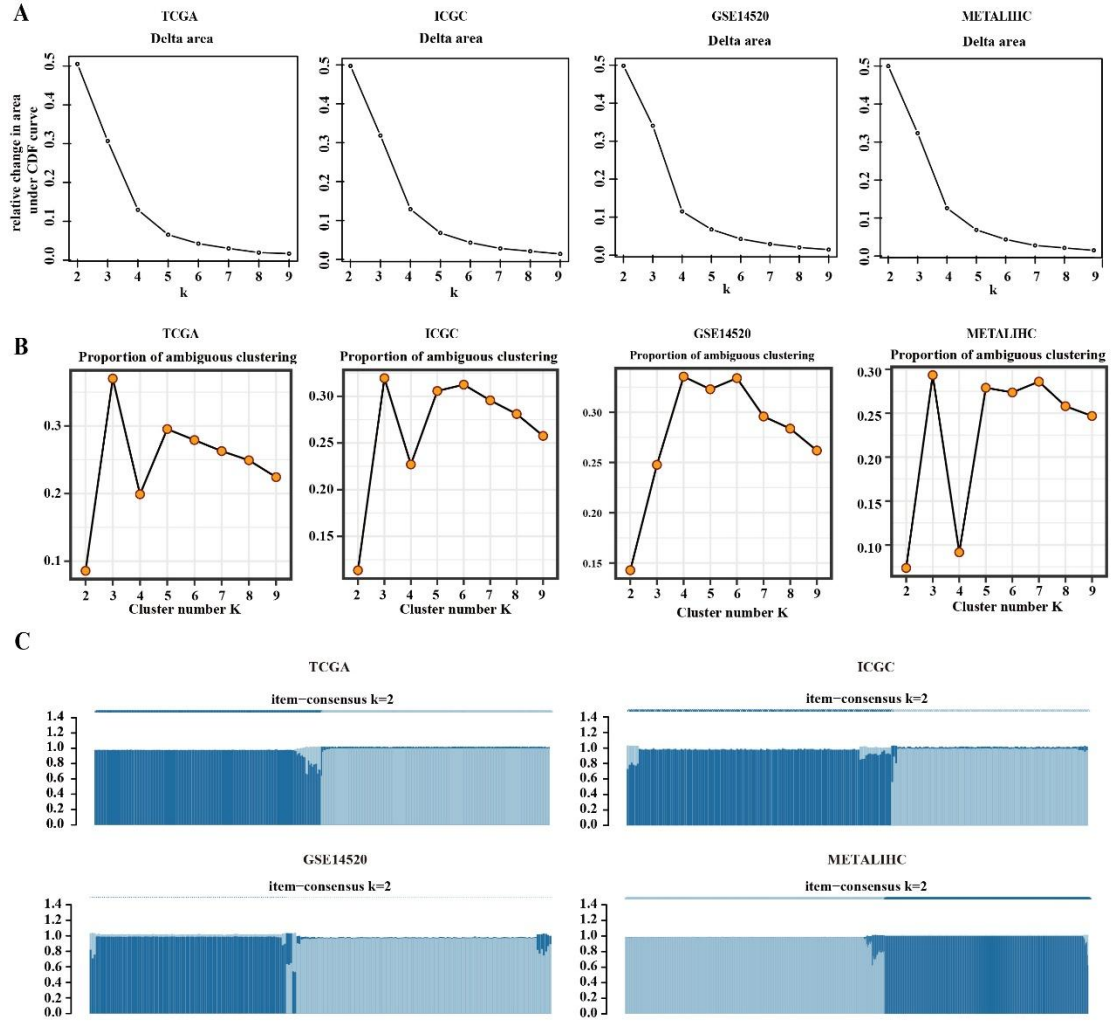


Fig. S10. Consensus clustering analysis of TCGA, ICGC, GSE14520, and METALLIC datasets. (A) Delta Area plot showing the relative increase in the CDF area for each cluster number (k). A marked increase is observed from $k = 2$ to $k = 3$, after which the gain plateaus, indicating a stable clustering structure at $k = 2$. (B) Proportion of Ambiguous Clustering (PAC) scores across different values of k , with the lowest PAC value observed at $k = 2$, suggesting minimal clustering ambiguity and optimal cluster stability. (C) Distribution of item-consensus scores for each k , with the highest overall consistency observed at $k = 2$, reflecting stable clustering across subsampling iterations.

Table S1 Genes associated with programmed cell death and metabolism

Apoptosis	Apoptosis	Apoptosis	Apoptosis	Apoptosis	Apoptosis	Apoptosis	Apoptosis	Apoptosis	Pyroptosis	Ferroptosis
AATF	CLU	GCLM	MFF	PRDX2	TCF7L2	CCND1	IL1R1	PSMD13	BAK1	ABCC1
ABL1	COA8	GDNF	MIF	PRELID1	TERT	CCND2	IL1RAP	PSMD14	BAX	ACACA
ACAA2	COL2A1	GFRAL	MIR132	PRKCA	TFDP1	CD2	IL3	PSMD2	CASP1	ACO1
ACKR3	CRADD	GGCT	MIR15A	PRKCD	TFDP2	CD69	IL3RA	PSMD3	CASP3	ACSF2
ACVR1	CREB3	GHITM	MIR16-1	PRKDC	TFPT	CDC25B	IRAK1	PSMD4	CASP4	ACSL1
ACVR1B	CREB3L1	GNAI2	MIR17	PRKN	TGFB1	CDK2	IRAK2	PSMD5	CASP5	ACSL3
ADORA1	CRH	GNAI3	MIR198	PRKRA	TGFB2	CDKN1B	IRAK3	PSMD6	CASP6	ACSL4
AEN	CRIP1	GPBR1	MIR21	PRODH	TGFB1R1	CREBBP	IRAK4	PSMD7	CASP8	ACSL5
AGT	CSF2	GPX1	MIR210	PSEN1	THBS1	CTNBN1	MAP3K14	PSMD8	CASP9	ACSL6
AGTR2	CSNK2A1	GRINA	MIR221	PSMD10	TICAM1	DCN	MYD88	PSMD9	CHMP2A	AIFM2
AIFM1	CSNK2A2	GSDME	MIR222	PSME3	TICAM2	DFFA	NFKB1	PSME1	CHMP2B	AKR1C1
AKT1	CTH	GSK3A	MIR26B	PTEN	TIMM50	DNAJC3	NFKBIA	PSME2	CHMP3	AKR1C2
ANXA6	CTNNA1	GSK3B	MIR27B	PTGIS	TIMP3	DPYD	NTRK1	PSME4	CHMP4A	AKR1C3
APAF1	CTSC	GSKIP	MIR449A	PTH	TLR3	EBP	PIK3CA	PSMF1	CHMP4B	ALOX12
APPL1	CTTN	GSTP1	MKNK2	PTPMT1	TLR4	EGR3	PIK3CB	RPS27A	CHMP4C	ALOX15
AR	CUL1	GZMB	MLH1	PTPN1	TM2D1	EMP1	PIK3CD	SEM1	CHMP6	ALOX5
ARHGEF2	CUL2	HDAC1	MLLT11	PTPN2	TMBIM1	ENO2	PIK3CG	STAT3	CHMP7	ATG5
ARL6IP5	CUL3	HERPUD1	MMP9	PTPRC	TMBIM6	ERBB2	PIK3R2	STK26	CYCS	ATG7
ARMC10	CUL4A	HGF	MNT	PTTG1IP	TMC8	EREG	PIK3R3	TJP1	ELANE	ATP5MC3
ARRB2	CUL5	HIC1	MOAP1	PYCARD	TMEM102	ETF1	PIK3R5	TJP2	GPX4	BACH1
ASAH2	CX3CL1	HIF1A	MPV17L	QARS1	TMEM109	F2	PPP3CA	UBA52	GSDMB	CARS
ATF3	CX3CR1	HINT1	MSH2	RACK1	TMEM117	F2R	PPP3CB	UBC	GSDMC	CBS
ATF4	CXCL12	HIP1	MSH6	RAF1	TMEM14A	FDXR	PPP3R2	UNC5A	GSDMD	CD44
ATM	CYLD	HIP1R	MSX1	RB1	TMEM161A	FEZ1	PRKACA	VIM	GSDME	CHAC1
ATP2A1	CYP1B1	HIPK1	MUC1	RB1CC1	TNF	GADD45A	PRKACB		GZMB	CISD1
ATP2A3	DAB2IP	HIPK2	MUL1	RBCK1	TNFAIP3	GADD45B	PRKACG		HMGB1	CP
ATP5IF1	DAP	HMGB2	MYBBP1A	RELA	TNFRSF10A	GCH1	PRKAR1A		IL18	CRYAB
AVP	DAP3	HMOX1	NACC2	RET	TNFRSF10B	GNA15	PRKAR1B		IL1A	CS
BAD	DAPK1	HNRNPK	NANOS3	RFFL	TNFRSF10C	GPX3	PRKAR2A		IL1B	CYBB
BAG3	DAPK2	HRAS	NBN	RHOT1	TNFRSF12A	GPX4	PRKAR2B		IRF1	DPP4

BAG5	DAPK3	HRK	NCK1	RHOT2	TNFRSF1A	GSN	PRKX	IRF2	EMC2
BAG6	DAPL1	HSPA1A	NCK2	RIPK1	TNFRSF1B	GSR	TNFRSF10D	NLRC4	FADS2
BAK1	DAXX	HSPA1B	NDUFA13	RIPK3	TNFRSF25	GSTM1	ACIN1	NLRP1	FANCD2
BAX	DBH	HSPB1	NDUFS3	RNF183	TNFSF10	GUCY2D	APC	NLRP2	FDFT1
BBC3	DCC	HTRA2	NFATC4	RNF186	TNFSF12	H1-0	APIP	NLRP3	FTH1
BCAP31	DDIAS	HTT	NFE2L2	RNF34	TOPORS	IER3	ARHGAP10	NLRP6	FTL
BCL10	DDIT3	HYAL2	NGF	RNF41	TP53	IFITM3	AVEN	NLRP7	FTMT
BCL2	DDIT4	HYOU1	NGFR	RPL11	TP53BP2	IFNGR1	BMX	NOD1	G6PD
BCL2A1	DDX3X	ICAM1	NKX3-1	RPL26	TP63	IGF2R	C1QBP	PLCG1	GCLC
BCL2L1	DDX47	IFI16	NLE1	RPS27L	TP73	IGFBP6	CARD8	PJVK	GCLM
BCL2L10	DDX5	IFI27	NME5	RPS3	TPD52L1	IL18	CDH1	PRKACA	GLS2
BCL2L11	DEDD	IFI27L1	NMT1	RPS6KB1	TPT1	IL6	CDKN2A	PYCARD	GOT1
BCL2L12	DEDD2	IFI27L2	NOC2L	RPS7	TRADD	IRF1	CLSPN	SCAF11	GPX4
BCL2L14	DELE1	IFI6	NOG	RRP8	TRAF1	ISG20	DBNL	TINAP	GSS
BCL2L2	DEPTOR	IFNB1	NOL3	RTKN2	TRAF2	LEF1	DSG1	TNF	HMGCR
BCL3	DIABLO	IFNG	NONO	RTL10	TRAF7	LMNA	DSG2	TP53	HMOX1
BCLAF1	DIDO1	IGF1	NOS3	S100A8	TRAP1	LUM	DSG3	TP63	HSBP1
BDKRB2	DNAJA1	IKBKE	NOX1	S100A9	TRIAP1	MGMT	DSP	AIM2	HSPB1
BDNF	DNAJC10	IL12A	NR4A2	SCG2	TRIB3	MMP2	DYNLL1	GSDMA	IREB2
BECN1	DNM1L	IL19	NUPR1	SCN2A	TRIM32	NEDD9	DYNLL2	IL6	KEAP1
BID	DPF2	IL1A	OPA1	SCRT2	TRIM39	NEFH	FNTA	NOD2	LPCAT3
BIK	DYRK2	IL1B	P2RX4	SELENOK	TXNDC12	PAK1	GAS2	TIRAP	MAP1LC3A
BIRC6	E2F1	IL2	P2RX7	SELENOS	TYROBP	PDCD4	GSDMD		MAP1LC3B
BLOC1S2	E2F2	IL20RA	P4HB	SENP1	UACA	PDGFRB	H1-1		MAP1LC3C
BMF	EDA2R	IL33	PAK2	SEPTIN4	UBB	PLAT	H1-2		MT1G
BMP4	EIF2AK3	IL4	PAK5	SERINC3	UBE2K	PLCB2	H1-3		NCOA4
BMP5	ELL3	IL6R	PARK7	SERPINE1	UBE4B	PLPPR4	H1-4		NFE2L2
BMPR1B	ENO1	IL7	PARP1	SFN	UBQLN1	PPP2R5B	H1-5		NFS1
BNIP3	EP300	INCA1	PARP2	SFPQ	UMOD	PPT1	HMGB1		NOX1
BNIP3L	EPHA2	ING2	PAWR	SFRP1	UNC5B	PRF1	KPNA1		NQO1
BOK	EPO	ING5	PCGF2	SFRP2	URI1	PSEN2	KPNB1		NRF2
BRCA1	ERBB3	INHBA	PDCD10	SGMS1	USP28	PTK2	LMNB1		OTUB1
BRCA2	ERCC6	INHBB	PDCD5	SGPL1	USP47	RARA	MAGED1		PCBP1

BRSK2	ERN1	INS	PDCD6	SGPP1	VDAC2	RETSAT	MAPK1	PCBP2
BTK	ERN2	ITGA6	PDIA3	SH3RF1	VNN1	RHOB	MAPK3	PEBP1
CAAP1	ERO1A	ITGAM	PDK1	SHH	WDR35	RNASEL	MAPT	PGD
CASP1	ERP29	ITGAV	PDK2	SHISA5	WNT4	ROCK1	OCLN	PHKG2
CASP10	EYA1	ITM2C	PDPK1	SIAH1	WWOX	SAT1	OMA1	PRNP
CASP12	EYA2	ITPR1	PDX1	SIAH2	XBP1	SATB1	PKP1	PROM2
CASP2	EYA3	ITPRIP	PEA15	SIRT1	YAP1	SC5D	PLEC	PTGS2
CASP3	EYA4	IVNS1ABP	PELI3	SIVA1	YBX3	SLC20A1	PRKCQ	RPL8
CASP4	FADD	JAK2	PERP	SKIL	YWHAB	SMAD7	PSMA1	SAT1
CASP5	FAF1	JMY	PF4	SLC25A5	YWHAE	SPTAN1	PSMA2	SAT2
CASP8	FAIM	JUN	PHIP	SLC35F6	YWHAG	SQSTM1	PSMA3	SLC11A2
CASP8AP2	FAIM2	KDM1A	PHLDA3	SLC9A3R1	YWHAH	TAP1	PSMA4	SLC1A5
CASP9	FAM162A	KITLG	PIAS4	SMAD3	YWHAQ	TGFBR3	PSMA5	SLC39A14
CAV1	FAS	KRT18	PIDD1	SNAI1	YWHAZ	TIMP1	PSMA6	SLC39A8
CCAR2	FASLG	KRT8	PIH1D1	SNAI2	ZC3HC1	TIMP2	PSMA7	SLC3A2
CCK	FASTK	LCK	PIK3R1	SNW1	ZDHHC3	TOP2A	PSMA8	SLC40A1
CD14	FBH1	LGALS12	PINK1	SOD1	ZMYND11	TSPO	PSMB1	SLC7A11
CD24	FBXW7	LGALS3	PLAGL2	SOD2	ZNF205	TXNIP	PSMB10	SQLE
CD27	FEM1B	LRRK2	PLAUR	SORT1	ZNF385A	WEE1	PSMB11	STEAP3
CD28	FGA	LTBR	PLEKHF1	SP100	ZNF385B	XIAP	PSMB2	TF
CD38	FGB	LY96	PLSCR3	SRC	ZNF622	AKT2	PSMB3	TFRC
CD3E	FGF10	MADD	PMAIP1	SRPX	ZSWIM2	AKT3	PSMB4	TP53
CD44	FGFR1	MAEL	PML	SST	ADD1	BIRC2	PSMB5	VDAC2
CD5	FGFR3	MAGEA3	POLB	SSTR3	AIFM3	CAPN1	PSMB6	VDAC3
CD70	FGG	MAP2K5	POU4F1	ST20	ANKH	CAPN2	PSMB7	ZEB1
CD74	FHIT	MAP3K5	POU4F2	STK11	ANXA1	CHP1	PSMB8	NOX3
CDIP1	FIGNL1	MAPK7	PPARD	STK24	APP	CHP2	PSMB9	NOX4
CDKN1A	FIS1	MAPK8	PPIA	STK25	AVPR1A	CHUK	PSMC1	NOX5
CDKN2D	FNIP2	MAPK8IP1	PPIF	STK3	BGN	CSF2RB	PSMC2	DUOX1
CEBPB	FXN	MAPK8IP2	PPM1F	STK4	BIRC3	CYCS	PSMC3	DUOX2
CFLAR	FYN	MAPK9	PPP1CA	STRADB	BMP2	DFFB	PSMC4	NRAS
CHAC1	FZD9	MARCHF7	PPP1R13B	STX4	BTG2	ENDOD1	PSMC5	KRAS
CHCHD10	G0S2	MAZ	PPP1R15A	STYXL1	BTG3	ENDOG	PSMC6	HRAS

CHEK2	GABARAP	MCL1	PPP2R1B	SYVN1	CASP6	EXOGEN	PSMD1		ALOX12B
CIB1	GATA1	MDM2	PPP3CC	TAF9	CASP7	IKBKB	PSMD11		ALOX15B
CIDEB	GATA4	MELK	PPP3R1	TAF9B	CCNA1	IKBKG	PSMD12		ALOXE3

Table S1 Genes associated with programmed cell death and metabolism (Continued)

Ferroptosis	Ferroptosis	Ferroptosis	Ferroptosis	Autophagy	Autophagy	Autophagy	Autophagy	Autophagy	Autophagy	Necroptosis
EGFR	circPSEN1	NCOA3	RARRES2	ABL1	FLCN	NPRL2	TBC1D25	CAPN2	RAF1	GLUD1
MAPK3	YAP1	NR5A2	USP11	ABL2	FOXK1	NRBP2	TBK1	CASP4	RB1	GLUD2
MAPK1	TRIM26	MTOR	RB1	ACER2	FOXK2	NUPR1	TEX264	CASP8	RELA	ALOX15
SOCS1	NDRG1	PANX2	HSPA5	ADRA1A	FOXO1	OPTN	TFEB	CCL2	RGS19	FTH1
CDO1	MIR302A	TFAP2A	HELLS	ADRB2	FOXO3	ORMDL3	TICAM1	CCR2	RPS6KB1	PYG
MYB	ASMTL-AS1	ARF6	MIR137	AKT1	FTH1	OSBPL7	TIGAR	CD46	SAR1A	CAPN1
LINC00472	LIFR	GDF15	SESN2	AMBRA1	FTL	PAFAH1B2	TLK2	CDKN1A	SERPINA1	CASP1
PRKAA2	PTPN6	ABHD12	ARNTL	ATF6	FYCO1	PARK7	TMEM150A	CDKN1B	SPHK1	GLNA
PRKAA1	ADAM23	TFAM	JUN	ATG101	FZD5	PHB2	TMEM150B	CDKN2A	SPNS1	BAX
BAP1	ARHGEF26-AS1	KDM3B	TMBIM4	ATG13	GAPDH	PHF23	TMEM150C	CFLAR	ST13	BCL2
MIR6852	CPEB1	RNF113A	PLIN2	ATG14	GATA4	PIK3C2A	TMEM39A	CHMP2B	TM9SF1	FADD
ACVR1B	MIR15A	PARK7	ZFP36	ATG2A	GBA	PIK3C3	TMEM39B	CTSB	TMEM49	RIPK1
TGFBR1	MIB1	AHCY	PIR	ATG2B	GFAP	PIK3CA	TMEM59	CTSD	TMEM74	TNF
TNFAIP3	MIR539	circ-TTBK2	HCAR1	ATG5	GNAI3	PIK3CB	TOMM7	CTSL1	TNFSF10	TNFRSF1A
ATF3	CDKN2A	MIR522	SLC16A1	ATG7	GOLGA2	PIK3R2	TP53	CX3CL1	TP63	TRADD
ATM	ANO6	PPARA	FZD7	ATM	GPR137	PIM2	TP53INP1	CXCR4	TP73	TRAF2
IDH1	HMGB1	SIAH2	FNDCC5	ATP13A2	GPR137B	PINK1	TP53INP2	DIRAS3	TUSC1	PPIA
TAFAZZIN	YY1AP1	NEDD4	GLRX5	ATP6V0A1	GPSM1	PIP4K2A	TPCN1	DLC1	ULK2	CAPN2

BECN1	EGLN2	PRDX1	RHEBP1	ATP6V0A 2	GSK3A	PIP4K2B	TPCN2	DNAJB1	ULK3	HSP90A
LONP1	MIOX	AR	IDH2	ATP6V0B	GSK3B	PIP4K2C	TREM2	DNAJB9	VAMP3	IL1A
CD82	MTDH	CHMP5	TYRO3	ATP6V0C	HAX1	PJVK	TRIB3	EDEM1	VAMP7	TNFSF6
CYB5R1	PANX1	CHMP6	ECH1	ATP6V0D 1	HDAC6	PLEKHF1	TRIM13	EEF2	VEGFA	TNFRSF6
ELOVL5	IL1B	MTF1	SOX2	ATP6V0D 2	HERC1	PLK2	TRIM14	EEF2K	WDR45	CASP8
FADS1	CTSB	COPZ1	FURIN	ATP6V0E 1	HGF	PLK3	TRIM21	EGFR	WDR45L	JNK
FBXW7	ATF4	NUPR1	circGFRA 1	ATP6V0E 2	HIF1A	POLDIP2	TRIM22	EIF2AK2	WIP1	JAK2
PTEN	LINC00618	USP35	TMSB4X	ATP6V1A	HMGB1	PRKAA1	TRIM27	EIF2AK3	ZFYVE1	CAMK2
MT1DP	PEX10	HSF1	TMSB4Y	ATP6V1B 1	HMOX1	PRKAA2	TRIM34	EIF2S1		IL1B
AGPAT3	LIG3	PLA2G6		ATP6V1B 2	HSP90AA 1	PRKAB1	TRIM38	EIF4EBP1		IFNG
PEX12	SIRT1	HIF1A		ATP6V1C 1	HSPA8	PRKAB2	TRIM5	ERBB2		STAT3
CHP1	PVT1	NEAT1		ATP6V1C 2	HSPB1	PRKACA	TRIM6	ERO1L		IRF9
GPAT4	BRD7	PARP1		ATP6V1D	HSPB8	PRKAG1	TRIM65	FADD		TNFSF10
BRPF1	SLC25A28	PARP2		ATP6V1E 1	HTR2B	PRKAG2	TRIM68	FAM48A		TNFRSF10 A
OSBPL9	TSC1	PARP3		ATP6V1E 2	HTRA2	PRKAG3	TRIM8	FAS		TNFRSF10 B
INTS2	IFNA1	PARP4		ATP6V1G 1	HTT	PRKD1	TRIML1	FKBP1A		CFLAR
MMD	IFNA2	PARP6		ATP6V1G 2	HUWE1	PRKN	TRIML2	FKBP1B		XIAP
CYP4F8	IFNA4	PARP8		ATP6V1H	IFI16	PSAP	TSC1	FOS		BID
MLLT1	IFNA5	PARP9		AUP1	IFNG	PTPN22	TSC2	acid		AIFM1

TTPA	IFNA6	PARP10	BAD	IKBKG	PYCARD	TSPO	GABARA P	TRPM7
GRIA3	IFNA7	PARP11	BAG3	IL10	QSOX1	UBA5	GABARA PL1	IFNAR1
EPT1	IFNA8	PARP12	BCL2	IL10RA	RAB39B	UBQLN1	GABARA PL2	IFNAR2
POM121L12	IFNA10	PARP14	BCL2L11	IL4	RAB3GA P1	UBQLN2	GNB2L1	IFNGR1
AEBP2	IFNA13	PARP15	BECN1	IRGM	RAB3GA P2	UBQLN4	GOPC	IFNGR2
AGPS	IFNA14	PARP16	BMF	ITPR1	RAB7A	UCHL1	GRID1	TLR3
CDCA3	IFNA16	PDSS2	BNIP3	KAT5	RAB8A	UFC1	GRID2	TIRP
PEX2	IFNA17	OIP5-AS1	BNIP3L	KAT8	RALB	UFL1	HDAC1	IFNA
PEX6	IFNA21	MIR190A	BOK	KDM4A	RASIP1	UFM1	HGS	IFNB
TIMM9	CircKDM4C	CREB1	C9orf72	KDR	RB1CC1	ULK1	HSP90AB 1	TRIF
DCAF7	GJA1	CREB3	CALCOC O2	KEAP1	RETREG1	USP10	HSPA5	VDAC1
LCE2C	PIEZO1	CREB5	CAMKK2	KIF25	RETREG3	USP13	IKBKB	SLC25A4S
FAR1	KDM6B	MIR130B	CAPN1	KLHL22	RHEB	USP30	IKBKE	PPID
PHF21A	KDM5C	BEX1	CAPNS1	KLHL3	RIPK2	USP33	IL24	CYLD
SMAD7	CCDC6	FABP4	CASP1	LACRT	RMC1	USP36	ITGA3	RIPK3
LYRM1	CARS1	AKT1S1	CASP3	LAMP1	RNF152	UVRAG	ITGA6	MLKL
AMN	miR-182-5p	MLST8	CDC37	LAMP2	RNF41	VDAC1	ITGB1	TRAF5
PEX3	miR-378a-3p	CDH1	CDK5	LAMP3	RNF5	VPS13C	ITGB4	TLR4
MTCH1	ZFAS1	SIRT6	CDK5R1	LAMTOR 1	ROCK1	VPS13D	GAA	RBCK1
ACADSB	SLC38A1	KIF20A	CHMP4A	LAMTOR 2	RPTOR	VPS26A	KIAA0226	HMGB1
hsa_circ_00083 67	TLR4	circRHOT1	CHMP4B	LAMTOR 3	RRAGA	VPS26B	KIAA0652	JAK1
GSK3B	METTTL14	ETV4	CISD2	LAMTOR 4	RRAGB	VPS35	KIAA0831	JAK3

MAPK8	MUC1	MEG8	CLEC16A	LAMTOR 5	RRAGC	WAC	KIF5B	TYK2
TGFB1	SCD	VCP	CLN3	LARP1	RRAGD	WASHC1	KLHL24	STAT1
SNCA	SRC	circ_000714 2	CLU	LEP	RUBCN	WDFY3	MAP2K7	STAT2
CGAS	STAT3	RBMS1	CPTP	LEPR	RUFY4	WDR24	MAPK1	STAT4
STING1	PML	KDM4A	CSNK2A2	LGALS8	SCFD1	WDR41	MAPK8IP 1	STAT5A
HDDC3	TP63	MGST1	CTSA	LRRK2	SCOC	WDR6	MAPK9	STAT5B
MIR761	CDKN1A	circKIF4A	CTTN	LRSAM1	SEC22B	WDR81	MBTPS2	STAT6
MDM2	FH	miR-7-5p	DAP	LZTS1	SESN1	WIPI2	MTMR14	H2A
MDM4	CISD2	circ_006793 4	DAPK1	MAP1LC3 A	SESN2	ZC3H12A	MYC	TNFAIP3
POR	MIR9-1	MPC1	DAPK2	MAP1LC3 B	SESN3	ZKSCAN3	NAF1	RNF31
MIR214	MIR9-2	CAMKK2	DAPK3	MAP1LC3 C	SH3BP4	ZMPSTE2 4	NAMPT	CHMP2A
DLD	MIR9-3	SRSF9	DAPL1	MAP3K7	SH3GLB1	APOL1	NBR1	CHMP2B
DNAJB6	SQSTM1	MIR4443	DCN	MAPK15	SIRT1	ARNT	NCKAP1	VPS24
WWTR1	ISCU	MIR27A	DDIT3	MAPK3	SIRT2	ARSA	NFE2L2	CHMP4A
PRKCA	LINC00336	MIR670	DDRGK1	MAPK8	SLC38A9	ARSB	NFKB1	CHMP4B
IFNG	BRD4	MEF2C	DEPDC5	MAPT	SMCR8	ATF4	NKX2-3	CHMP6
SMPD1	PRDX6	NF2	DEPP1	MCL1	SMG1	ATG10	NLRC4	VPS4
MYCN	MIR17	EZH2	DHRX	MEFV	SNCA	ATG12	NRG1	CHMP1
SMG9	CA9	PEDS1	DNM1L	MET	SNRNP70	ATG16L1	NRG2	CHMP5
IL6	LAMP2	CDC25A	DRAM1	MFN2	SNX32	ATG16L2	NRG3	SMPD1
PAQR3	GCH1	CAV1	DRAM2	MFSD8	SNX5	ATG3	P4HB	PYCARD
MICU1	RRM2	LCN2	EEF1A1	MID2	SNX6	ATG4A	PARK2	NLRP3
TOR2A	NR4A1	TRIB2	EEF1A2	MIR199A 1	SOGA1	ATG4B	PARP1	ZBP1
MIR375	PIK3CA	DHODH	EIF2AK4	MIRLET7 B	SOGA3	ATG4C	PEA15	IL33
SIRT3	RPTOR	MIR545	EIF4G1	MLST8	SPTLC1	ATG4D	PELP1	FTL

MIR324	SREBF1	PDK4	EIF4G2	MT3	SPTLC2	ATG9A	PEX14	SQSTM1
QSOX1	SREBF2	CircPVT1	ELAPOR1	MTCL1	SQSTM1	ATG9B	PEX3	VDAC2
CLTRN	P4HB	circDTL	EP300	MTDH	SREBF1	ATIC	PIK3R4	VDAC3
KLF2	BCAT2	PTPN18	EPM2A	MTM1	SREBF2	BAG1	PPP1R15A	CHMP7
MIR5096	MIR424	ABCC5	ERCC4	MTMR3	STAT3	BAK1	PRKAR1A	PGAM5
H19	FXN	CISD3	ERN1	MTMR4	STBD1	BAX	PRKCD	BIRC2
ELAVL1	SUV39H1	circRHBG	EXOC1	MTMR8	STING1	BCL2L1	PRKCQ	BIRC3
YTHDC2	ATF2	GALNT14	EXOC4	MTMR9	STK11	BID	PTEN	EIF2AK2
DDR2	STK11	KLHDC3	EXOC7	MTOR	STUB1	BIRC5	PTK6	PLA2G4
SLC39A7	CircIL4R	LINC01833	EXOC8	NCOA4	SUPT5H	BIRC6	RAB11A	DNM1L
TRIM46	NEDD4L	GSTM1	FBXL2	NEDD4	SVIP	BNIP1	RAB1A	SPATA2
KDM5A	BRD2	circ0097009	FBXO7	NLRP6	SYNPO2	C12orf44	RAB24	FAF1
CYGB	BRD3	TMEM161B-DT	FBXW7	NOD1	TAB2	C17orf88	RAB33B	SHARPIN
GSTZ1	BRDT	circEPSTI1	FEZ1	NOD2	TAB3	CANX	RAB5A	NOX2
CIRBP	DECR1	MIR18A	FEZ2	NPC1	TBC1D14	CAPN10	RAC1	USP21

Table S1 Genes associated with programmed cell death and metabolism (Continued)

Necroptosis	Cuproptosis	Parthanatos	Entoticcell death	Netoticcell death	Lysosome-dependentcelldeath	Lysosome-dependentcelldeath	Lysosome-dependentcelldeath	Alkalip tosis	Oxeip tosis	NETo sis
PARP1	NFE2L2	PARP	AMPK	ELANE	ABCA2	GCC2	SORL1	IKBKB	PGAM5	MYD88
CHMP4C	NLRP3	MIF	ATG5	MMP1	ABCB9	GGA1	SORT1	NFKB1	KEAP1	TLR2
SPATA2L	ATP7B	AIFM1	ATG7	MPO	ACP2	GGA2	SPAG9	CA9	AIFM1	PAD4
CYBB	ATP7A	HSP70	BECN1	CAMP	ACP5	GGA3	SPHK2	CHUK	NRF2	PRKCA
CAMK2A	SLC31A1	PAAN	CDC42	PADI4	ADGRE2	GLA	SQSTM1	IKBKG	AIRE	PKCB

CAMK2D	FDX1	ARH3	CDH1	EIPA	AGA	GLB1	STXBP1	NFKB1 A	PRKC Z
CAMK2B	LIAS	RNF146	CTNNA1	NCX1	AP1B1	GM2A	STXBP2	RELA	NOX3
CAMK2G	LIPT1	ADPRH L2	CYBB	MIA	AP1G1	GNPTAB	SUMF1		NOX4
SLC25A4	LIPT2	OGG1	MYH14		AP1M1	GNPTG	SYK		NOX1
SLC25A5	DLD		PI3KC3		AP1M2	GNS	SYTL4		CTSG
SLC25A6	DLAT		RHOA		AP1S1	GUSB	TCIRG1		PRTN 3
SLC25A31	PDHA1		RNF146		AP1S2	HDAC6	TFEB		ELAN E
GLUL	PDHB		ROCK		AP1S3	HEXA	TMEM106B		MPO
PYGL	MTF1		RUBCN		AP3B1	HEXB	TPP1		GSD MD
PYGM	GLS		UVRAG		AP3B2	HGS	UNC13D		IL1B
PYGB	CDKN2 A				AP3D1	HGSNAT	VAMP7		CXCL 1
MAPK8	DBT				AP3M1	HMOX1	VAMP8		PLA2 G7
MAPK10	GCSH				AP3M2	HPS6	VPS33A		CXCL 8
MAPK9	DLST				AP3S1	HSPA8	VPS33B		CDK6
PLA2G4E					AP3S2	HYAL1	VPS4A		HMG B1
PLA2G4A					AP4B1	IDS	WASH3P		MMP 9
JMJD7- PLA2G4B					AP4E1	IDUA	ZFYVE16		AGER
PLA2G4B					AP4M1	IGF2R			CSF3
PLA2G4C					AP4S1	IL13			TGFB 1
PLA2G4D					ARF1	IL13RA2			
PLA2G4F					ARL8B	IL4			

CHMP3	ARSA	IL4R
RNF103-	ARSB	KIF1B
CHMP3	ARSG	KIT
VPS4B	ASAH1	KXD1
VPS4A	ATP10B	LAMP1
CHMP1B	ATP13A2	LAMP2
CHMP1A	ATP6AP1	LAMP3
FASLG	ATP6V0A1	LAMTOR1
FAS	ATP6V0A2	LAPTM4A
IFNA1	ATP6V0A4	LAPTM4B
IFNA2	ATP6V0B	LAPTM5
IFNA4	ATP6V0C	LAT
IFNA5	ATP6V0D1	LAT2
IFNA6	ATP6V0D2	LGALS9
IFNA7	ATP6V1H	LGMN
IFNA8	BLK	LIPA
IFNA10	BLOC1S1	LRRK2
IFNA13	BLOC1S2	LYN
IFNA14	BORCS5	M6PR
IFNA16	BORCS6	MAN2B1
IFNA17	BTK	MANBA
IFNA21	C12orf4	MAP1LC3A
IFNB1	CBL	MAP6
TICAM2	CD164	MCOLN1
TICAM1	CD300A	MFSD8
HSP90AA1	CD63	MILR1
HSP90AB1	CD68	MRGPRX2
H2AX	CD84	MT3
H2AC20	CHGA	MYH9
H2AC12	CLN3	NAGA
H2AC1	CLN5	NAGLU
H2AC25	CLNK	NAGPA
H2AB3		

H2AC8	CLTA	NAPSA
H2AC4	CLTB	NCOA4
MACROH 2A2	CLTC	NDEL1
MACROH 2A1	CLTCL1	NEDD4
H2AC19	CLU	NEU1
H2AJ	CPLX2	NPC1
H2AB1	CTNS	NPC2
H2AC17	CTSA	NR4A3
H2AC18	CTSB	PDPK1
H2AC11	CTSC	PIK3C3
H2AC21	CTSD	PIK3CD
H2AZ2	CTSE	PIK3CG
H2AC7	CTSF	PIP4K2A
H2AZ1	CTSG	PIP4K2B
H2AC15	CTSH	PIP4P1
H2AC6	CTSK	PLA2G15
H2AC13	CTSL	PLA2G3
H2AC14	CTSO	PLEKHM1
H2AC16	CTSS	PLEKHM2
H2AB2	CTSV	PPT1
H2AL3	CTSW	PPT2
	CTSZ	PSAP
	DEF8	PSAPL1
	DNASE2	PTGDR
	DNASE2B	PTGDS
	ENTPD4	RAB34
	FAM98A	RAB3A
	FER	RAB7A
	FES	RAC2
	FGR	RUBCNL
	FLCN	S100A13

FOXF1	SCARB2
FTH1	SGSH
FTL	SLC11A1
FUCA1	SLC11A2
GAA	SLC17A5
GAB2	SMPD1
GALC	SNAP23
GALNS	SNAPIN
GATA2	SNX16
GBA	SNX4

Table S1 Genes associated with programmed cell death and metabolism (Continued)

Immunogenic cell death	Anoikis	Anoikis	Anoikis	Anoikis	Paraptosis	Methuosis	Entosis	Disulfidptosis	Metabolism	Metabolism
ATG5	BRMS1	CDKN3	FASLG	RBL2	CAMK2B	CSNK2A1	AR	SLC7A11	HK3	TALDO1
BAX	PTK2	CBL	AFP	SIRPA	PRKACG	RAC1	TP53	NADPH	HK1	RPIA
CALR	NTRK2	CASP9	ITGA8	TRAF2	MARK4	ARF6	ROCK1	SLC3A2	HK2	SHPK
CASP1	BCL2L11	SFN	NOX4	ADCY10	SSTR5	GIT1	PCK2	RPN1	HKDC1	DERA
CASP8	SRC	MTDH	PBK	VPS37A	TAAR5	MTOR	TNFSF10	NCKAP1	GCK	RBKS
CD4	CEACAM6	PRKCA	SATB1	TNFRSF12A	USP10	MET	MTUS2	GLUT1	GPI	PRPS1L1
CD8A	CAV1	TNFRSF10B	CD63	APOBEC3G	PRKAG3	PFKFB3	AURKA	FLNA	PFKM	PRPS2
CD8B	AKT1	CXCL8	EEF1A1	BAG1	HACD2	MIR199A1	KIF2C	FLNB	PFKP	PRPS1
CXCR3	ITGB1	MIR200C	LTB4R2	COL13A1	NT5C		RHOA	MYH9	PFKL	RGN
EIF2AK3	CEACAM5	AR	MAVS	MNX1	INSRR		MTOR	TLN1	FBP1	IDNK
ENTPD1	EGFR	CDKN2A	HRC	RAD9A	SSTR3		EZR	ACTB	FBP2	GLYCTK
FOXP3	BCL2	CPT1A	CCN2	IFI27	TAAR9		GZMB	MYL6	ALDOC	GUSB
HMGB1	CASP8	PIK3CB	RHOB	MEGF11	HSPB8		MRTFA	MYH10	ALDOA	KL

HSP90AA1	SIK1	CLDN1	PPP1R13 B	ITPRIP	PLPP2	PTK2	CAPZB	ALDOB	UGT2A1
IFNA1	PTRH2	MIR204	PLG	BCL2L15	G6PC2	DIAPH1	DSTN	TPI1	UGT2A3
IFNB1	STAT3	MIR26A1	MET	SNAI2	GUCY2E P	LPAR2	IQGAP1	GAPDH	UGT2B17
IFNG	TLE1	CDKN1A	RAF1	PTPN1	CDK4	MAP1LC3 A	ACTN4	GAPDHS	UGT2B11
IFNGR1	DAPK2	CDKN1B	PARP1	NOTCH3	RGR	PIKFYVE	PDLIM1	PGK2	UGT2B28
IL10	CTNNB1	KLF12	PRKCQ	GLUD1	ADGRG1	CTTN	CD2AP	PGK1	UGT1A6
IL17A	ZNF304	NTRK1	BRCA2	SIRT1	UQCRC1	MCOLN1	INF2	PGAM1	UGT1A4
IL17RA	MAPK1	PLAU	RB1	FASN	TNK2	FOXO1	WASF2	PGAM2	UGT1A1
IL1B	BMF	MYC	SP1	MYH9	RNF181	CTNNA1	CYFIP1	PGAM4	UGT1A3
IL1R1	ITGA5	SMAD4	HAVCR2	RPS6KB1	MKNK2	CXCL8	ABI2	ENO3	UGT2B10
IL6	TP53	PLK1	DOCK1	TPM1	UBE2U		BRK1	ENO2	UGT1A9
LY96	MCL1	MUC1	VTN	PPP2R1A	MYLK		RAC1	ENO1	UGT2B7
MYD88	BCL2L1	LGALS1	INHBB	COL4A2	CTDSP2		GYS1	ENO4	UGT1A10
NLRP3	CASP3	PYCARD	PDCD4	CTNND1	LCK		NDUFA11,	PKM	UGT1A8
NT5E	CDH1	SESN2	PRPF4B	CD151	GPR15		LRPPRC	PKLR	UGT1A5
P2RX7	BAD	ITGB3	RANBP9	MMP11	ATP23		NCKAP1	PDHA2	UGT2B15
PDIA3	PIK3CA	KRAS	SESN1	ARHGEF7	LPAR1		NDUFS1	PDHA1	UGT1A7
PIK3CA	PAK1	THBS1	SESN3	PPP2R2A	PI4KB		PPM1F	PDHB	UGT2B4
PRF1	ITGAV	BID	CD24	SEMA7A	DSTYK		CNOT1	DLAT	UGT2A2
TLR4	FN1	HRAS	ZBTB7A	PPP2R5A	CFD		NDUFC1	DLD	UGDH
TNF	MAPK3	CDK11B	MIR141	BST2	PPP3CA		NDUFA10	LDHAL6 A	UGP2
	PTGS2	CDK11A	ELANE	CCN1	CCR4		NUBPL	LDHAL6 B	CRYL1
	BAX	XIAP	KDR	PPP2R2D	PRAG1		NDUFS2	LDHA	XYLB
	BCAR1	PPARG	MDM2	CCDC178	CDKN3		EPAS1	LDHB	AKR1B1
	PTEN	IL6	NFE2L2	MIR10A	GPR153		OXSM	LDHC	AKR1B10
	ERBB2	MIR145	ZEB1	MIR30B	DDIT3		CCNC	ADH1A	AKR1B15
	ANGPTL4	CCR7	KL	MIR30C1	MAPK8		OXSM	ADH1B	DCXR
	PDK4	MSLN	PRKCI	SHC1	MAP2K2			ADH1C	SORD

CYCS	RAC1	CRYAB	MAPK1	ADH7	DHDH
BRAF	GRHL2	EPHB6	MAPK14	ADH4	FGGY
YAP1	BIRC3	FGF2	IGF1R	ADH5	CRPPA
ANKRD13 C	NOTCH1	HK2	PDCD6IP	ADH6	MPI
ITGA2	RHOG	LTF	CASP9	AKR1A1	PMM2
ANXA5	CCAR2	IQGAP1	ERN1	ALDH2	PMM1
BIRC5	NQO1	MGAT5	ATF6	ALDH3A 2	GMPPB
MTOR	MMP13	SDCBP	XBP1	ALDH1B 1	GMPPA
TIMP1	FAS	ABHD2	AKT1	ALDH7A 1	GMDS
BDNF	MTA1	SPIB	EIF2S1	ALDH9A 1	GFUS
CSPG4	MYO5A	TRIM31	HSPA5	ALDH3B 1	FPGT
BSG	EDA2R	MIR1827	CASP4	ALDH3B 2	FCSK
AKT2	CCN6	PDGFRB	CASP3	ALDH3A 1	ENOSF1
STK11	MMP9	PLAT	CASP7	ACSS1	PFKFB1
IGF1	ABL1	TLR3	ITPR3	ACSS2	PFKFB2
IGF1R	MAPK11	NRAS	RYR1	GALM	PFKFB3
ITGA6	SOD2	ROCK1	RYR2	PGM1	PFKFB4
ILK	PTHLH	PAK4	MCU	PGM2	TIGAR
CFLAR	PDGFB	VEGFA	TNFRSF1 9	G6PC1	KHK
RHOA	GLI2	CASP10	PDCD5	G6PC2	TKFC
HIF1A	EZH2	PIN1	CSF1	G6PC3	GALK1
DAP3	RIPK1	IL1RAP	TP53	ADPGK	GALT
MYBBP1A	CXCR4	UBE2C	NFKB1	BPGM	GALE
TLE5	HMGA1	YWHAZ	PEBP1	MINPP1	GLB1

ITGA3	SIK2	TWIST1	PHB	PCK1	LCT
PTK2B	TNFSF10	BMP6		PCK2	LALBA
CCND1	ANGPTL2	BNIP3L		CS	B4GALT 1
CTTN	S100A4	ELK1		ACLY	B4GALT 2
CALR	NTF3	KDM3A		ACO2	GLA
ATF4	ETV4	PRDX4		ACO1	MGAM
CDCP1	MIR21	BNIP3		IDH1	MGAM2
PLAUR	MIR124-1	LMO3		IDH2	GAA
SKP2	HTRA1	ZNF32		IDH3B	GANC
CHEK2	LATS1	MIR200B		IDH3G	SI
HGF	CEACAM3	MIR525		IDH3A	MIOX
E2F1	EIF2AK3	MIR363		OGDHL	ACACA
EGF	LAMC2	TUBB3		OGDH	ACACB
PIK3CG	LAMA3	HSP90B1		DLST	ACSF3
ITGB4	LAMB3	SLC2A1		SUCLG1	MCAT
DAPK1	CDH2	HMOX1		SUCLG2	FASN
MAPK8	CSNK2A1	PTPN11		SUCLA2	OXSM
PIK3R1	EDIL3	PRKACA		SDHA	CBR4
PIK3R3	ZEB2	PAK3		SDHB	HSD17B8
MAP2K1	TLN1	CD36		SDHC	HTD2
CXCL12	EPHA2	PIK3R2		SDHD	MECR
LGALS3	SIRT3	PPP2CA		FH	OLAH
FBXW7- AS1	OLFM3	CASP6		MDH1	ACSL6
BAK1	CLU	CDH3		MDH2	ACSL4
ABHD4	SPINK1	EEF2K		PC	ACSL1
CD44	CPEB2	LRP1		G6PD	ACSL5
ITGA4	NAT1	PAK2		PGLS	ACSL3
FADD	TSG101	PTK6		H6PD	ACSBG1
PHLDA2	MIR200A	LPAR1		PGD	ACSBG2
TGFB1	MIR6744	TCF7L2		RPE	ACAA2

HMCN1	SERPINA1	CEACAM1	RPEL1	HADHB
MMP2	AKT3	GDF2	TKT	HADH
CEBPB	RELA	GLO1	TKTL2	HADHA
CEMIP	TNFRSF1A	IL17A	TKTL1	ECHS1
			HYAL1	SPAM1

Table S1 Genes associated with programmed cell death and metabolism (Continued)

Metabolism	Metabolism	Metabolism	Metabolism	Metabolism	Metabolism	Metabolism	Metabolism	Metabolism	Metabolism
PPT2	CYP11B2	COX8C	NME2	CYP2A6	BCAT1	LAP3	NAT8	GALNT12	CSGALNACT2
ELOVL1	HSD11B1	COX8A	NME4	CYP2A7	GCLC	P4HA2	GSR	GALNT13	CHSY3
ELOVL2	HSD11B1L	COX11	NME1	CAD	GCLM	P4HA3	TXNDC12	GALNT14	CHSY1
ELOVL3	HSD11B2	COX15	NME3	DHODH	GSS	P4HA1	GPX4	GALNT16	CHPF
ELOVL4	AKR1C1	COX17	NME1-NME2	UMPS	CDO1	PRODH2	GPX6	GALNT15	CHPF2
ELOVL5	SULT1E1	CYCS	AK9	CMPK1	MPST	HOGA1	GPX7	GALNT18	DSE
ELOVL6	HSD17B1	ATP5F1A	ENTPD3	CMPK2	TST	L3HYPDH	GPX2	GALNTL5	DSEL
ELOVL7	HSD17B2	ATP5F1B	ENTPD8	ASMTL	BCKDHA	HAL	GPX3	GALNT10	CHST11
HSD17B12	HSD17B6	ATP5F1C	ENTPD1	CTPS1	BCKDHB	UROC1	GPX1	GALNT2	CHST12
HACD2	DHRS11	ATP5F1D	CANT1	CTPS2	DBT	AMDHD1	GPX5	GALNT3	CHST13
HACD1	CYP1A1	ATP5F1E	ENTPD4	UCK1	IVD	FTCD	GPX8	GALNT1	CHST3
HACD4	CYP1A2	ATP5PO	ENTPD5	UCK2	ACAD8	HDC	PRDX6	GALNT6	CHST7
HACD3	CYP3A5	ATP6	ENTPD6	UCKL1	HSD17B10	HNMT	GBA3	GALNT4	CHST15
TECR	CYP3A7	ATP5PB	NUDT16	UPP2	PCCA	CARNMT1	GYS2	GALNT9	UST
ACOT4	CYP3A7-CYP3A51P	ATP5MC1	ITPA	UPP1	PCCB	HGD	GYS1	GALNT7	CHST14
ACOT2	CYP2E1	ATP5MC2	XDH	NT5C3A	MCEE	GSTZ1	GYG1	GALNT8	B3GNT2
ACOT1	CYP3A4	ATP5MC3	NUDT2	NT5C3B	MMUT	FAH	GYG2	POC1B-GALNT4	CHST6
ACOT7	CYP1B1	ATP5PD	GMPS	CDA	HIBCH	TYR	GBE1	C1GALT1	B4GALT4

THEM4	CYP19A1	ATP5ME	GMPR	DCTPP1	HIBADH	TH	PYGL	C1GALT1C1	B3GNT7
THEM5	HSD17B11	ATP5MF	GMPR2	DCTD	ALDH6A1	DCT	PYGM	C1GALT1C1L	CHST1
ACAT2	COMT	ATP5MG	GDA	DTYMK	AOX1	TYRP1	PYGB	GCNT1	CHST2
ACAT1	LRTOMT	ATP5PF	GUK1	DUT	MCCC1	DDC	AGL	GCNT3	CHST4
ACAA1	HSD17B3	ATP8	RRM1	TYMP	MCCC2	DBH	AMY1C	GCNT4	EXTL2
EHHADH	ND1	ATP6V1A	RRM2B	TK2	AUH	PNMT	AMY2A	ST3GAL1	EXTL3
ACOX3	ND2	ATP6V1B1	RRM2	TK1	HMGCL	TPO	AMY1A	ST3GAL2	EXTL1
ACOX1	ND3	ATP6V1B2	HDDC2	TYMS	HMGCLL1	FAHD1	AMY2B	ST6GALNAC1	EXT1
ACADS	ND4	ATP6V1C2	DGUOK	DPYD	OXCT1	MIF	AMY1B	ST6GALNAC2	EXT2
ACADM	ND4L	ATP6V1C1	DCK	DPYS	OXCT2	PAH	TREH	ST6GALNAC3	NDST1
ACADL	ND5	ATP6V1D	HDDC3	UPB1	AACS	TDO2	PGM2L1	ST6GALNAC4	NDST2
ACADSB	ND6	ATP6V1E2	PRUNE1	IL4I1	HMGCS1	IDO1	DOLK	B3GNT3	NDST3
ACADVL	NDUFS1	ATP6V1E1	ADCY1	DDO	HMGCS2	IDO2	DPAGT1	B3GNT6	NDST4
GCDH	NDUFS2	ATP6V1F	ADCY2	ASRGL1	AASS	AFMID	ALG5	B4GALT5	GLCE
CPT1A	NDUFS3	ATP6V1G1	ADCY3	ASNS	AADAT	KMO	ALG13	ST3GAL3	HS2ST1
CPT1B	NDUFS4	ATP6V1G3	ADCY4	NIT2	DHTKD1	KYNU	ALG14	B4GALNT3	HS6ST1
CPT1C	NDUFS5	ATP6V1G2	ADCY5	AGXT	HYKK	HAAO	DPM1	B4GALNT4	HS6ST2
CPT2	NDUFS6	ATP6V1H	ADCY6	AGXT2	PHYKPL	ACMSD	DPM2	CHST8	HS6ST3
ECI1	NDUFS7	TCIRG1	ADCY7	NAT8L	CAMKMT	ALDH8A1	DPM3	CHST9	HS3ST1
ECI2	NDUFS8	ATP6V0A2	ADCY8	RIMKLB	KMT2A	TPH2	ALG1	OGT	HS3ST2
CYP2U1	NDUFV1	ATP6V0A4	ADCY9	RIMKLA	KMT2D	TPH1	ALG2	EOGT	HS3ST3B1
FDFT1	NDUFV2	ATP6V0A1	ADCY10	FOLH1	KMT2C	ASMT	ALG11	POFUT1	HS3ST3A1
SQLE	NDUFV3	ATP6V0C	GUCY1A2	ASPA	KMT2B	AANAT	ALG3	POFUT2	HS3ST5
LSS	NDUFA1	ATP6V0B	GUCY1A1	GAD1	KMT2E	INMT	ALG9	MFNG	GK2
CYP51A1	NDUFA2	ATP6V0D1	GUCY1B1	GAD2	SETD1B	CAT	ALG12	LFNG	GK
TM7SF2	NDUFA3	ATP6V0D2	GUCY2C	ABAT	SETD1A	GADL1	ALG6	RFNG	GPAM
LBR	NDUFA4	ATP6V0E1	GUCY2D	ALDH5A1	SETD7	CSAD	ALG8	B3GLCT	GPAT2
MSMO1	NDUFA4L2	ATP6V0E2	GUCY2F	ALDH4A1	PRDM9	MLYCD	ALG10	POGLUT1	GPAT4
NSDHL	NDUFA5	ATP6AP1	NPR1	GFPT2	PRDM7	ADO	ALG10B	GXYLT1	GPAT3
HSD17B7	NDUFA6	ATP4A	NPR2	GFPT1	ASH1L	FMO1	STT3A	GXYLT2	AGPAT1
EBP	NDUFA7	ATP4B	PDE1A	SHMT2	SMYD2	FMO2	STT3B	XXYLT1	AGPAT2
DHCR24	NDUFA8	ATP12A	PDE1B	SHMT1	SMYD3	FMO5	RPN1	POMT1	AGPAT3
SC5D	NDUFA9	PPA2	PDE1C	GRHPR	SMYD1	FMO3	RPN2	POMT2	AGPAT4

DHCR7	NDUFA10	PPA1	PDE2A	PHGDH	SUV39H1	FMO4	DAD1	POMGNT1	AGPAT5
LIPA	NDUFAB1	LHPP	PDE3A	PSAT1	SUV39H2	GGT7	DDOST	B3GAT1	LCLAT1
CEL	NDUFA11	OTC	PDE3B	PSPH	EHMT2	GGT6	MAGT1	B3GAT2	MBOAT1
SOAT2	NDUFA12	ASS1	PDE5A	GCAT	EHMT1	GGT1	TUSC3	CHST10	MBOAT2
SOAT1	NDUFA13	ASL	PDE6A	ALAS1	SETDB1	GGT5	OSTC	FUT9	PLPP1
CYP2R1	NDUFB1	ARG2	PDE6B	ALAS2	SETDB2	PCYT2	TMEM258	FUT4	PLPP3
CYP27B1	NDUFB2	ARG1	PDE6C	MAOB	PRDM2	SELENOI	DOLPP1	POMGNT2	PLPP2
CYP24A1	NDUFB3	NOS1	PDE6D	MAOA	EZH1	CEPT1	MOGS	B3GALNT2	LPIN1
CYP46A1	NDUFB4	NOS2	PDE6G	AOC3	EZH2	PCYT1B	GANAB	POMK	LPIN3
CYP39A1	NDUFB5	NOS3	PDE6H	AOC2	SETMAR	PCYT1A	MAN1B1	FKTN	LPIN2
HSD3B7	NDUFB6	GLS2	PDE9A	GLDC	NSD1	CHPT1	MAN1A2	FKRP	PLPP5
CH25H	NDUFB7	GLS	PDE10A	AMT	NSD2	SCLY	MAN1C1	RXYLT1	PLPP4
CYP7B1	NDUFB8	GLUL	PDE11A	GCSH	NSD3	TXNRD1	MAN1A1	B4GAT1	DGKZ
CYP7A1	NDUFB9	GLUD2	ADSS1	DAO	SETD2	TXNRD3	MGAT1	LARGE1	DGKD
CYP27A1	NDUFB10	GLUD1	ADSS2	GATM	DOT1L	TXNRD2	MAN2A1	LARGE2	DGKI
CYP8B1	NDUFB11	CPS1	AMPD2	GAMT	KMT5A	SEPHS2	MAN2A2	CHIA	DGKA
AKR1D1	NDUFC1	GOT1	AMPD3	CHDH	PRDM6	SEPHS1	MGAT2	CHIT1	DGKE
AKR1C4	NDUFC2	GOT1L1	AMPD1	BHMT	KMT5C	PSTK	FUT8	NAGK	DGKB
SLC27A5	NDUFC2-KCTD14	GOT2	ADK	DMGDH	KMT5B	SEPSECS	B4GALT3	AMDHD2	DGKH
AMACR	UQCRFS1	GPT2	ADA	PIPOX	MECOM	MARS1	ST6GAL1	GNPDA1	DGKG
ACOX2	CYTB	GPT	ADA2	SARDH	PRDM16	MARS2	ST6GAL2	GNPDA2	DGKQ
HSD17B4	CYC1	NAGS	AK7	GNMT	TMLHE	DGLUCY	MGAT3	GNPNAT1	DGKK
SCP2	UQCRC1	ACY1	AK4	CBS	BBOX1	GGCT	MGAT4A	PGM3	DGAT1
ACOT8	UQCRC2	ABHD14A-ACY1	AK5	CTH	PLOD1	CHAC1	MGAT4B	GALK2	DGAT2
BAAT	UQCRH	NUDT9	AK2	SDS	PLOD2	CHAC2	MGAT4D	UAP1	MOGAT3
TAT	UQCRHL	ADPRM	AK1	SDSL	PLOD3	OPLAH	MGAT5	UAP1L1	PNPLA2
COQ2	UQCRB	NUDT5	AK8	SRR	COLGALT1	ANPEP	MGAT5B	GNE	PNPLA3
COQ6	UQCRQ	PPAT	AK6	KYAT3	COLGALT2	GSTA5	MGAT4C	RENBP	PNLIP
COQ3	UQCR10	GART	AK3	KYAT1	CKM	GSTA2	NEU1	NANS	PNLIPRP1

COQ5	UQCR11	PFAS	ENTPD2	BHMT2	CKMT1A	GSTA4	NEU3	NANP	PNLIPRP2
COQ7	COX10	PAICS	NTPCR	MTR	CKMT2	GSTO2	NEU4	NPL	PNLIPRP3
NQO1	COX3	ADSL	ENPP1	MAT2B	CKB	GSTM4	NEU2	CMA5	LIPC
GGCX	COX1	ATIC	ENPP3	MAT1A	CKMT1B	GSTT2	HEXA	CYB5R1	LIPF
VKORC1	COX2	APRT	PDE4A	MAT2A	AZIN2	GSTT1	HEXB	CYB5R3	LIPG
VKORC1L1	COX4I2	NT5C2	PDE4B	AMD1	ODC1	GSTM3	HEXD	CYB5R2	LPL
HPD	COX4I1	NT5C1A	PDE4C	SRM	AOC1	MGST1	MAN2C1	CYB5RL	AGK
CYP11A1	COX5A	NT5C1B	PDE4D	SMS	SMOX	MGST3	MAN2B1	CYB5R4	MGLL
CYP17A1	COX5B	NT5C	PDE7A	MTAP	CNDP1	GSTM1	MAN2B2	UXS1	ABHD16A
STS	COX6A1	NT5M	PDE7B	MRI1	CNDP2	GSTM5	MANBA	HYAL2	MOGAT1
SULT2B1	COX6A2	NT5C1B- RDH14	PDE8B	APIP	CARNS1	MGST2	ENGASE	PPT1	NAGLU
CYP21A2	COX6B1	NT5DC4	PDE8A	ENOPH1	SAT2	GSTA1	FUCA1	CYP11B1	GALNS
HSD3B1	COX6B2	NT5E	FHIT	ADI1	SAT1	GSTM2	FUCA2	COX7C	GNS
HSD3B2	COX6C	PNP	ENPP4	DNMT1	AGMAT	GSTA3	AGA	NME7	XYLT1
SRD5A1	COX7A1	LACC1	PAPSS2	DNMT3A	OAT	GSTO1	GBA1	NAT1	XYLT2
SRD5A2	COX7A2	HPRT1	PAPSS1	DNMT3B	PYCR3	GSTT2B	GBA2	BCAT2	B4GALT7
SRD5A3	COX7A2L	IMPDH1	URAD	AHCYL2	PYCR2	GSTP1	GALNTL6	ALDH18A1	B3GALT6
AKR1C2	COX7B	IMPDH2	ALLC	AHCYL1	PYCR1	GSTK1	GALNT5	LANCL1	B3GAT3
AKR1C3	COX7B2	NME6	NAT2	AHCY	PRODH	HPGDS	GALNT17	GALNT11	CSGALNACT 1
HYAL4	HYAL3	IDS	IDUA	ARSB	HPSE	HPSE2	SGSH	HGSNAT	

Table S2 Comprehensive overview of datasets utilized in the present study.

No.	Dataset	Normal	HCC	Platform	Database
1	TCGA-LIHC	50	356	Illumina HiSeq 2000	TCGA
2	ICGC-LIRI-JP	-	232	Illumina HiSeq 2000	ICGC
3	GSE14520	-	211	Affymetrix Human Genome U133A 2.0 Array	GEO
4	GSE151530	-	25	Illumina NovaSeq 6000	GEO
5	GSE149614	-	10	Illumina NovaSeq 6000	GEO
6	GSE125449	-	9	Illumina NextSeq 500	GEO
7	GSE156625	-	14	Illumina HiSeq 2500	GEO
8	GSE100797		25	Illumina HiSeq 2000	TIGER
9	GSE91061	-	58	Illumina Genome Analyzer	TIGER
10	PRJ	-	91	-	TIGER
11	RCC	-	281	Illumina HiSeq 2000 or 2500	TIGER
12	Phs	-	150	-	TIGER
13	Nanth	-	24	-	TIGER
14	GSE20742	-	30	Illumina NovaSeq 6000	GEO

Table S3 Co-expressed genes between programmed cell death and metabolism identified by earson correlation analysis

Genes	Genes	Genes	Genes	Genes	Genes	Genes	Genes
FTL	RPL8	GAPDH	CALR	HSP90AB1	GLUL	MAT1A	CD63
HSP90B1	NDUFB7	PLG	ENO1	GRINA	COX6B1	SLC25A6	ADH1B
DAD1	HSP90AA1	PSMB4	PRDX1	RPN2	PDIA3	PSMB3	RPS27A
CANX	COX8A	LGALS1	RPS3	NDUFS6	CYC1	UBA52	ACSL1
BCAP31	AKR1C3	ATP6V0E1	PMVK	PSMD4	MYH9	FASN	RPS7
CAPNS1	TALDO1	PTGES3	UQCRH	SQSTM1	GPAA1	PSMB5	DPM3
CHMP2A	AKR1C1	RNF181	COX6C	ANXA5	CHMP4B	CERS2	LAMTOR2
PGK1	NQO1	AKR1C2	ATP6V1F	LMNA	ACTN4	MGAT4B	CLTA
MTCH1	PPIA	DYNLL1	PEA15	ATP6V0B	ACADSB	YWHAZ	HMGA1
PGD	LAMTOR4	YWHAH	TKT	SRM	IDI1	ALDH6A1	GSDMD
AP1S1	VIM	HEXB	CTNNA1	GNS	SHARPIN	PPP1CA	CLTC
TXNRD1	ATP6V1E1	NDUFA2	LAMTOR1	PSMC5	PSMD3	NDUFA3	PKM
ATP6AP1	NONO	CD46	PLOD3	S100A4	ALG3	SQLE	PDCD5
COASY	GBA	FLNA	SMS	FDPS	BAX	HMGB2	CYCS
FKBP1A	IL6R	PPT1	HACD2	DEGS1	PIH1D1	GM2A	ABHD12
RHEB	ITGA5	UQCRB	LAMTOR5	HSF1	PRKAB2	SPTAN1	KIF5B
PHB	FLAD1	IFNGR2	G6PD	CD4	ATP6V1C1	COL4A2	SMYD2
PIR	PSMD11	TAP1	DTYMK	WASF2	NDUFB9	TIMM9	STX4
CDK4	PDGFRB	PAFAH1B3	GGCT	DCAF7	ITGA6	CAV1	HYAL2
DRAM2	ITGAV	PHLDA2	TIMM50	PTGES2	PARP1	DCN	NT5C
PSMD14	MFF	TFPT	PIGT	UQCR11	VPS35	NME1	PGP
MCOLN1	BLOC1S1	GJA1	PTK2	RIPK2	GSTZ1	TREM2	NOTCH3
LGALS9	IFI27L2	PSMA1	SLC38A1	RGS19	PLA2G7	GLA	IL3RA
CTSC	CHMP3	GMPPB	ST6GALNAC4	APIP	UACA	HDCC2	
PCBP1	SLC2A1	HEXA	PLAT	PIK3R3	CCND2	ENTPD1	
ADCY3	ALDOA	BCAT1	CHST12	NDUFA13	NDUFA11	ABI2	

Table S4 Identification of 106 prognostic genes from PCD-Metabolism co-expressed genes in HCC using univariate cox regression

Genes	Genes	Genes	Genes	Genes
FTL	RPL8	GAPDH	HSP90AB1	CD63
ENO1	ADH1B	DAD1	HSP90AA1	PSMB4
PRDX1	RPN2	RPS27A	LGALS1	AKR1C3
ATP6V0E1	PSMD4	RPS7	TALDO1	PTGES3
UQCRH	SQSTM1	GPAA1	PSMB5	ANXA5
CHMP4B	PGK1	NQO1	ATP6V1F	CLTA
MTCH1	PPIA	DYNLL1	PEA15	ATP6V0B
YWHAZ	HMGA1	PGD	YWHAH	TKT
SRM	HEXB	CTNNA1	GNS	SHARPIN
CLTC	TXNRD1	ATP6V1E1	LAMTOR1	PSMC5
PKM	ATP6AP1	NONO	PLOD3	ALG3
PDCD5	COASY	GBA	SMS	HMGB2
FKBP1A	PPT1	DEGS1	GM2A	ABHD12
RHEB	ITGA5	LAMTOR5	HSF1	KIF5B
PHB	FLAD1	IFNGR2	G6PD	ATP6V1C1
PSMD11	DTYMK	WASF2	TIMM9	CDK4
PAFAH1B3	DCAF7	DRAM2	ITGAV	PHLDA2
TIMM50	NT5C	PSMD14	MFF	PIGT
VPS35	RIPK2	TREM2	SLC38A1	
PLA2G7	GLA	CTSC	CHMP3	
APIP	HDDC2	SLC2A1	ABI2	
CHST12	RGS19	ST6GALNAC4	BCAT1	

Table S5 The machine learning algorithms used by PCD-Metabolism were 117 different combinations

Model	TCGA	ICGC	GSE14520	Meta	Average C-index
StepCox[both] + RSF	0.929	0.758	0.673	0.813	0.793
StepCox[backward] + RSF	0.929	0.758	0.673	0.813	0.793
RSF	0.935	0.754	0.651	0.81	0.787
StepCox[forward] + RSF	0.935	0.754	0.651	0.81	0.787
StepCox [both] + GBM	0.888	0.770	0.656	0.792	0.776
StepCox [backward] + GBM	0.888	0.770	0.656	0.792	0.776
Lasso + RSF	0.912	0.733	0.638	0.781	0.766
StepCox[forward] + GBM	0.834	0.760	0.665	0.767	0.756
GBM	0.834	0.760	0.665	0.767	0.756
CoxBoost + GBM	0.787	0.745	0.665	0.741	0.734
Lasso + GBM	0.779	0.738	0.648	0.729	0.723
Enet [$\alpha=0.2$]	0.744	0.766	0.640	0.715	0.716
StepCox[forward] + Enet [$\alpha=0.2$]	0.744	0.766	0.640	0.715	0.716
Enet [$\alpha=0.1$]	0.740	0.763	0.646	0.715	0.716
StepCox[forward] + Enet [$\alpha=0.1$]	0.740	0.763	0.646	0.715	0.716
Enet [$\alpha=0.3$]	0.743	0.765	0.642	0.715	0.716
StepCox[forward] + Enet [$\alpha=0.3$]	0.743	0.765	0.642	0.715	0.716
Enet [$\alpha=0.4$]	0.741	0.765	0.641	0.714	0.715
StepCox[forward] + Enet [$\alpha=0.4$]	0.741	0.765	0.641	0.714	0.715
Enet [$\alpha=0.5$]	0.742	0.767	0.638	0.714	0.715
StepCox[forward] + Enet [$\alpha=0.5$]	0.742	0.767	0.638	0.714	0.715
RSF + GBM	0.784	0.720	0.625	0.719	0.712
StepCox [forward] + Ridge	0.732	0.752	0.649	0.710	0.711
Ridge	0.758	0.750	0.613	0.709	0.708
CoxBoost + plsRcox	0.703	0.749	0.656	0.696	0.701
Enet [$\alpha=0.7$]	0.705	0.744	0.659	0.697	0.701
StepCox[forward] + Enet [$\alpha=0.7$]	0.705	0.744	0.659	0.697	0.701
Lasso + StepCox [forward]	0.704	0.744	0.659	0.697	0.701
Enet [$\alpha=0.6$]	0.705	0.741	0.660	0.697	0.701
StepCox[forward] + Enet [$\alpha=0.6$]	0.705	0.741	0.660	0.697	0.701
CoxBoost + Enet [$\alpha=0.4$]	0.705	0.744	0.658	0.697	0.701

CoxBoost + Enet [$\alpha=0.5$]	0.705	0.744	0.657	0.697	0.701
Lasso + plsRcox	0.704	0.742	0.659	0.697	0.701
CoxBoost + Enet [$\alpha=0.2$]	0.706	0.737	0.662	0.698	0.701
CoxBoost + Enet [$\alpha=0.6$]	0.705	0.743	0.658	0.697	0.701
CoxBoost + Enet [$\alpha=0.3$]	0.705	0.742	0.658	0.697	0.701
CoxBoost + Enet [$\alpha=0.7$]	0.705	0.743	0.658	0.696	0.701
CoxBoost + Enet [$\alpha=0.9$]	0.705	0.743	0.658	0.696	0.701
CoxBoost + Lasso	0.705	0.743	0.657	0.696	0.701
CoxBoost + Enet [$\alpha=0.8$]	0.705	0.743	0.657	0.696	0.700
CoxBoost + StepCox [forward]	0.702	0.750	0.654	0.696	0.700
Enet [$\alpha=0.9$]	0.705	0.743	0.657	0.697	0.700
StepCox[forward] + Enet [$\alpha=0.9$]	0.705	0.743	0.657	0.697	0.700
Enet [$\alpha=0.8$]	0.704	0.743	0.657	0.696	0.700
StepCox[forward] + Enet [$\alpha=0.8$]	0.704	0.743	0.657	0.696	0.700
StepCox[forward] + Lasso	0.704	0.743	0.656	0.696	0.700
Lasso	0.704	0.743	0.656	0.696	0.700
CoxBoost + Enet [$\alpha=0.1$]	0.706	0.733	0.663	0.698	0.700
Lasso + CoxBoost	0.706	0.741	0.656	0.696	0.700
Lasso + survival-SVM	0.704	0.743	0.654	0.696	0.699
StepCox[forward] + CoxBoost	0.706	0.738	0.657	0.696	0.699
CoxBoost	0.706	0.738	0.657	0.696	0.699
CoxBoost + survival-SVM	0.704	0.734	0.662	0.696	0.699
CoxBoost + Ridge	0.706	0.726	0.663	0.697	0.698
StepCox [both] + Ridge	0.752	0.739	0.601	0.699	0.698
StepCox [backward] + Ridge	0.752	0.739	0.601	0.699	0.698
StepCox [both] + Enet [$\alpha=0.1$]	0.752	0.738	0.599	0.698	0.697
StepCox [backward] + Enet [$\alpha=0.1$]	0.752	0.738	0.599	0.698	0.697
Lasso + SuperPC	0.704	0.733	0.655	0.694	0.696
StepCox [both] + Enet [$\alpha=0.2$]	0.753	0.737	0.598	0.697	0.696
StepCox [backward] + Enet [$\alpha=0.2$]	0.753	0.737	0.598	0.697	0.696
CoxBoost + SuperPC	0.703	0.722	0.665	0.695	0.696
StepCox [both] + Enet [$\alpha=0.3$]	0.753	0.737	0.597	0.697	0.696
StepCox [backward] + Enet [$\alpha=0.3$]	0.753	0.737	0.597	0.697	0.696

CoxBoost + StepCox [both]	0.704	0.734	0.654	0.692	0.696
CoxBoost + StepCox [backward]	0.704	0.734	0.654	0.692	0.696
Lasso + StepCox [both]	0.704	0.734	0.654	0.692	0.696
Lasso + StepCox [backward]	0.704	0.734	0.654	0.692	0.696
StepCox [both] + CoxBoost	0.753	0.737	0.596	0.696	0.695
StepCox [backward] + CoxBoost	0.753	0.737	0.596	0.696	0.695
StepCox [both] + Enet [$\alpha=0.4$]	0.753	0.736	0.596	0.696	0.695
StepCox [backward] + Enet [$\alpha=0.4$]	0.753	0.736	0.596	0.696	0.695
StepCox [both] + Enet [$\alpha=0.5$]	0.753	0.736	0.596	0.696	0.695
StepCox [backward] + Enet [$\alpha=0.5$]	0.753	0.736	0.596	0.696	0.695
StepCox [both] + Enet [$\alpha=0.6$]	0.752	0.737	0.595	0.695	0.695
StepCox [backward] + Enet [$\alpha=0.6$]	0.752	0.737	0.595	0.695	0.695
StepCox [both] + Enet [$\alpha=0.7$]	0.752	0.737	0.595	0.695	0.695
StepCox [backward] + Enet [$\alpha=0.7$]	0.752	0.737	0.595	0.695	0.695
StepCox [both] + Enet [$\alpha=0.8$]	0.752	0.737	0.594	0.695	0.695
StepCox [backward] + Enet [$\alpha=0.8$]	0.752	0.737	0.594	0.695	0.695
StepCox [both] + Enet [$\alpha=0.9$]	0.752	0.737	0.594	0.695	0.694
StepCox [backward] + Enet [$\alpha=0.9$]	0.752	0.737	0.594	0.695	0.694
StepCox[both] + Lasso	0.752	0.736	0.594	0.695	0.694
StepCox [backward] + Lasso	0.752	0.736	0.594	0.695	0.694
StepCox[forward] + plsRcox	0.762	0.728	0.590	0.695	0.694
plsRcox	0.747	0.722	0.607	0.697	0.693
StepCox[forward]	0.760	0.733	0.584	0.693	0.692
StepCox[both] + plsRcox	0.751	0.732	0.591	0.693	0.692
StepCox[backward] + plsRcox	0.751	0.732	0.591	0.693	0.692
StepCox[both]	0.751	0.732	0.591	0.693	0.692
StepCox[backward]	0.751	0.732	0.591	0.693	0.692
StepCox[both] + SuperPC	0.704	0.702	0.660	0.690	0.689
StepCox[backward] + SuperPC	0.704	0.702	0.660	0.690	0.689
StepCox[forward] + survival-SVM	0.684	0.705	0.673	0.685	0.687
survival - SVM	0.684	0.705	0.673	0.685	0.687
StepCox [both] + survival-SVM	0.684	0.700	0.675	0.684	0.686
StepCox [backward] + survival-SVM	0.684	0.700	0.675	0.684	0.686

StepCox[forward] + SuperPC	0.685	0.702	0.659	0.681	0.682
SuperPC	0.685	0.702	0.659	0.681	0.682
RSF + Ridge	0.689	0.669	0.661	0.677	0.674
RSF + Enet [$\alpha=0.1$]	0.687	0.666	0.659	0.676	0.672
RSF + StepCox [forward]	0.696	0.652	0.662	0.677	0.672
RSF + Enet [$\alpha=0.2$]	0.687	0.664	0.659	0.675	0.671
RSF + survival-SVM	0.676	0.677	0.656	0.672	0.670
RSF + plsRcox	0.696	0.651	0.659	0.675	0.670
RSF + Enet [$\alpha=0.3$]	0.687	0.661	0.657	0.675	0.670
RSF + Enet [$\alpha=0.4$]	0.687	0.660	0.658	0.675	0.670
RSF + StepCox [both]	0.694	0.647	0.662	0.676	0.670
RSF + StepCox [backward]	0.694	0.647	0.662	0.676	0.670
RSF + Enet [$\alpha=0.5$]	0.687	0.659	0.658	0.675	0.670
RSF + Enet [$\alpha=0.6$]	0.686	0.657	0.658	0.675	0.669
RSF + CoxBoost	0.686	0.657	0.659	0.675	0.669
RSF + Enet [$\alpha=0.7$]	0.686	0.657	0.658	0.675	0.669
RSF + Enet [$\alpha=0.9$]	0.686	0.656	0.659	0.674	0.669
RSF + Lasso	0.686	0.655	0.659	0.674	0.669
RSF + Enet [$\alpha=0.8$]	0.686	0.656	0.658	0.675	0.669
RSF + SuperPC	0.669	0.677	0.651	0.667	0.666

Table S6 Expression of PCD-metabolism model genes in wild-type and eight genetically engineered mouse models (log₂(TPM + 1))

	Aldoa	Cct3	Cdk4	Cks1b	Cnih4	Ctsc	Dab2	Eef1e1	Hdac2
AKTbcacat.2_S10	9.009535636	7.143039391	6.360241584	5.16738301	7.100023547	4.443141159	6.720867386	3.674091471	6.144711995
AKTbcacat.3_S15	7.256577436	6.903575496	5.402886377	4.571752422	6.843448729	4.964941684	6.72663694	3.443839788	5.624153039
AKTbcacat01_S2	7.419680776	6.938897795	5.668682062	4.945692002	7.410429303	4.828593716	6.686022814	4.13409851	5.761502473
AKTbcacat02_S4	7.466709779	6.330908798	5.401093521	4.624992488	7.629951343	5.438525997	6.064217925	4.206502012	5.512997999
AKTbcacat03_S7	8.516361584	7.087308826	5.994263052	4.999149638	7.39645655	4.678923566	5.985478139	4.026030061	5.711147173
AKThmet.1_S13	6.825480317	6.490662323	5.264239858	4.386082044	6.840291537	6.931842856	6.15942069	4.296318692	5.109980611
AKThmet.3_S3	6.661741981	6.448838291	5.527808949	4.661348517	6.864466239	6.813952011	6.993586644	3.621657236	5.448935616
AKThmet.4_S9	7.033135747	6.617995517	5.359655705	4.668415741	6.644327162	6.606752613	7.12241383	3.468973178	5.217395715
AKThmet.5_S6	6.787801607	6.520233263	5.430822837	4.676506296	6.715198366	6.942959365	7.022490682	3.612480276	5.405454673
AKThmet.6_S10	7.236694414	6.68905312	5.592389195	4.564286267	7.098487929	6.987023956	5.970243172	4.220061287	5.073637858
AKTNras.2_S1	7.751391639	7.018595413	6.554322595	5.74135617	6.675659387	6.59095687	6.956606672	4.206135673	5.817378644
AKTNras.3_S6	7.958162702	6.936245327	6.384806384	5.227133976	6.62923072	6.489756895	6.513659176	3.89028574	5.725490173
AKTNras.4_S8	7.609610994	6.835459425	6.647130411	5.621169961	7.075177147	6.79960906	6.528491056	4.651902203	5.848001383
AKTNras.5_S11	7.740398512	7.187007759	6.440670619	5.611360495	6.803673941	6.776977325	6.868390854	4.312944741	5.956615042
AKTNras.6_S10	8.33898161	7.312496661	6.942754789	6.069901349	6.961129156	6.638059893	6.663382652	4.378598057	6.209637942
cMyc.1_S10	9.490896273	8.950211016	8.333165744	7.521831804	7.597740537	4.287588513	7.007405041	6.329948371	7.07693409
cMyc.2_S13	8.23213191	8.569705185	7.94235668	7.112624135	7.57767114	4.817063722	5.988148231	5.901726943	6.794395492
cMyc.3_S4	8.330918198	8.496829012	7.555883581	6.194564582	6.662920305	4.730927174	5.015525833	5.642675166	6.564229121
cMyc.4_S5	9.205101519	9.102696679	8.428435294	8.116322489	7.525409099	4.93798053	5.451715094	6.588925336	6.763627701
cMyc.6_S5	8.916739362	9.197350599	8.246262511	8.028863805	8.157074629	5.556594327	4.560094757	7.160490081	6.985850321
hmetbcacat.1_S3	7.364091667	6.462028617	5.027114593	3.993507327	5.496809535	3.580770745	4.165502841	3.28020958	4.455941055
hmetbcacat.3_S5	6.335042692	6.438421788	5.00649679	3.845952095	5.940694878	4.126989338	4.7646096	3.150064635	4.431429298
hmetbcacat.4_S8	6.280800953	6.458110838	4.894048679	3.884841256	6.034306471	4.946902077	4.366323267	3.326848846	4.510859526
hmetbcacat.5_S2	7.225068679	6.811754706	5.37437449	4.765369438	6.474502183	5.336468738	5.915275354	3.420486749	4.95982891
hmetbcacat.6_S7	6.843233345	6.712531784	5.264179921	4.82103281	6.000551816	4.393670218	4.916610107	3.404853168	4.65376576
Nrf2bcacat.1_S4	7.664748419	7.034096087	4.974375972	5.136045824	6.49362089	5.359875935	4.804520578	4.117471915	4.963987557
Nrf2bcacat.2_S4	7.717503772	6.904178602	4.677745714	4.822870905	6.18847132	3.289298536	4.867251057	3.576762602	5.233543851
Nrf2bcacat.3_S9	7.390102111	6.9848902	4.779168335	5.012127326	6.264765597	4.475589802	5.229702356	3.945979184	5.067715666
Nrf2bcacat.4_S9	7.14630433	6.93107651	4.928752615	5.06391013	6.326568564	5.351370357	5.459777611	4.022108588	4.788312849
Nrf2bcacat.5_S4	9.292121109	7.26063102	4.755156444	5.247248507	5.962367408	4.419901857	5.844063355	3.944297504	5.307285296

sgAxin1hmet.3_S2	6.392807809	6.441916947	5.544012625	4.717842991	6.171658507	6.654073304	7.004625006	3.581531388	5.249342095
sgAxin1hmet.6_S7	5.771211789	5.892649373	4.534766111	4.45542836	5.974194107	5.905193374	5.623685212	3.495101164	5.384445574
sgAxin1hmet01_S12	5.911426124	6.035364488	4.672363351	4.115894576	6.335821938	6.132932702	5.32715038	3.69997878	4.602432256
sgAxin1hmet02_S2	6.006102906	6.347022964	5.393842729	4.811280718	6.652651494	6.942047489	6.285714121	4.060457096	4.737362582
sgAxin1hmet03_S8	5.688144482	6.2337444	4.952074667	4.399991305	6.635254478	6.254616325	5.33574709	3.873062749	4.44629933
sgPTENhmet.4_S14	6.048887555	5.832289094	4.840972512	3.757360893	5.533827826	6.493015875	5.484147357	3.249830254	4.807091448
sgPTENhmet.5_S2	6.025148739	5.893204964	4.983921676	4.099468152	5.46730364	6.263168036	5.343305224	3.447783828	4.755034468
sgPTENhmet.6_S3	6.208031601	5.894335235	4.809536669	3.507609539	5.412199514	6.537138919	5.516480004	3.233500402	4.609271796
sgPTENhmet02_S3	5.882631125	6.034863646	5.010876232	3.89116199	6.287961901	6.826653012	4.99970617	3.855359352	4.490890444
sgPTENhmet03_S8	5.672444195	5.788872867	4.892925012	3.842437939	6.279028065	7.007729039	5.050998635	4.263021964	4.305193186
WT.1_S1.y	5.585029228	6.042572208	4.540840698	3.596777156	5.598786522	6.165390121	4.858135537	3.047069341	4.629860603
WT.2_S7	5.17110357	5.858120773	4.188524735	3.369838825	5.99329697	6.54305382	5.355927783	3.617322027	4.59130084
WT.3_S13	5.193890951	5.903967849	4.338102985	3.487606809	5.948022644	6.40746035	4.979793289	3.647053125	4.6120751
WT.5_S9	5.005531409	5.748783915	4.034459277	3.542846451	5.730016931	6.14394842	5.339495134	3.562122604	4.967514334
WT01_S7	4.859108115	5.991261491	4.2990814	3.454479911	6.080457743	6.659506628	4.823907282	3.984253582	4.47048713

Table S6 Expression of PCD-metabolism model genes in wild-type and eight genetically engineered mouse models (log₂(TPM + 1)) (continued)

Mice	Hsp90b1	Ldha	Lgals3	Marcks	Pop7	Rcn2	Spp1	Stmn1	Tubb
AKTbcacat.2_S10	9.159094167	10.87404272	7.839685666	6.004572999	3.724857937	3.606344245	13.09371611	1.376439188	0.269611388
AKTbcacat.3_S15	8.98778929	10.47418135	7.295582143	4.771677668	3.13130038	2.927739675	10.8428405	1.007989437	0.931049424
AKTbcacat01_S2	8.90898732	10.55963215	7.715607815	5.966096646	3.696128973	3.696534107	12.46848353	1.01946286	0.263071581
AKTbcacat02_S4	8.675700624	10.81737052	8.061609875	5.79143177	3.566570356	3.152447749	11.78007467	0.966828108	0.242104513
AKTbcacat03_S7	8.656866371	10.7914163	8.716291885	5.915859798	3.941917036	3.04381533	12.79992388	0.950724159	0.32879846
AKThmet.1_S13	9.250800014	10.56685047	6.266167839	4.976960615	3.797444869	2.890165786	10.60910073	0.587013705	0.336521711
AKThmet.3_S3	9.352187371	10.76595399	6.664531865	5.577906728	3.630503275	3.348729116	11.97152762	0.389989879	0.221417019
AKThmet.4_S9	9.456590134	10.74821735	6.667604025	4.867104642	3.500195158	2.757997678	11.20822824	0.592351811	0.467553924
AKThmet.5_S6	9.47468066	10.70788141	6.577360447	5.240578136	3.491142222	3.207337507	11.70456378	0.817627541	0.444864217
AKThmet.6_S10	9.286010748	10.85410258	6.438653407	5.002532232	3.725145542	2.989006802	11.35448114	0.78422162	0.271261203
AKTNras.2_S1	9.130535872	10.55640923	6.584363916	5.776955693	3.999484017	3.97959105	13.58809806	1.027142995	0.193955628
AKTNras.3_S6	9.020691975	10.68698505	7.26326242	5.50583396	4.007446026	3.558897597	13.39310777	0.97836857	0.392070958
AKTNras.4_S8	9.310971755	10.74589824	7.059034066	5.882689952	4.08541369	4.14278342	13.71544371	0.710261762	0.154710781
AKTNras.5_S11	9.417691487	10.48223837	6.731163844	5.864675095	4.082758043	3.690921975	13.04882803	1.448808845	0.167841678
AKTNras.6_S10	9.292929658	10.55588671	7.568155144	6.288481011	4.181432565	4.064923325	13.34553692	0.908388739	0.169866035
cMyc.1_S10	9.730090183	11.96365135	8.303884047	6.022991127	4.062891326	4.671191254	6.477060376	2.216804814	0.232626635
cMyc.2_S13	9.555088724	11.73444466	6.737719777	6.589787042	3.881052044	4.623155675	5.428281099	2.255605314	1.161320696
cMyc.3_S4	8.603487117	11.22803367	7.93535407	5.029482208	3.781248818	3.140829584	4.691519071	1.603874237	0.174543109
cMyc.4_S5	10.05331839	11.71568461	7.977992002	6.829673916	4.130401077	3.735322911	3.822705427	1.812616517	0.197454196
cMyc.6_S5	9.915386524	11.75172866	8.76720961	7.647493736	3.95668887	4.169791301	4.397262325	1.742179047	0.221236151
hmetbcacat.1_S3	8.13461848	9.734235197	6.6793419	2.869771629	3.773628014	1.317204878	5.516293721	0.539277481	1.132903735
hmetbcacat.3_S5	9.081410498	10.53883509	5.314474702	3.198802763	3.300962958	1.708200894	6.97866391	0.5194769	0.407920551
hmetbcacat.4_S8	9.138396834	10.74564264	5.187768721	3.620070204	3.534040615	1.844973305	7.325222056	0.619628143	0.738282766
hmetbcacat.5_S2	9.619345465	10.79613949	7.678480922	4.076414022	3.783432878	2.176737856	7.784431989	0.809301423	0.516325175
hmetbcacat.6_S7	9.505154218	10.67343915	6.176276125	3.280896531	3.7914198	2.036807571	7.551458646	0.357545308	0.247308328
Nrf2bcacat.1_S4	8.855551938	10.2684752	6.207394111	4.160921601	3.645599791	1.545499892	4.524160225	0.983987497	0.655605676
Nrf2bcacat.2_S4	8.703082787	10.11038465	5.373578478	3.063836782	3.211572546	0.943626477	2.329583526	1.085010691	0.746094741
Nrf2bcacat.3_S9	8.829595968	10.12235616	4.936356502	3.634655312	3.176532331	1.123588323	3.892113203	1.257368146	0.245445345
Nrf2bcacat.4_S9	8.892342107	9.811473686	5.186129283	3.775241083	3.277021537	1.589258695	5.67448516	0.870990364	0.176921471

Nrf2bcat.5_S4	8.845391924	9.8901042	4.927001112	3.768201486	3.589118647	1.582178647	4.203898424	1.204098435	0.391267435
sgAxin1hmet.3_S2	9.203036439	10.36020269	6.235632258	5.45877381	2.905848397	3.027980454	9.591235716	0.782296109	0.20386564
sgAxin1hmet.6_S7	9.380071463	10.73573486	4.476304692	4.407153247	2.621875047	2.245691898	6.743322962	0.468024934	0.211846945
sgAxin1hmet01_S12	9.073921813	10.33195215	5.325986175	4.470659444	3.234206306	2.025796639	6.551580837	0.501680505	0.339456159
sgAxin1hmet02_S2	8.776960114	10.44948459	6.144423786	5.642905252	3.39821953	2.923953177	9.107083058	0.682323585	0.365016063
sgAxin1hmet03_S8	8.65178571	10.57454659	4.695828656	4.68226798	3.333817319	2.510079315	6.904041631	0.498449798	0.209705017
sgPTENhmet.4_S14	8.590077856	10.29837039	5.854346102	4.110469315	2.580016844	2.201487799	8.208682106	0.437704058	0.174679219
sgPTENhmet.5_S2	8.674331014	10.34897493	5.562063175	4.131452834	2.520947743	1.916754937	7.697642622	0.146368091	0.318658285
sgPTENhmet.6_S3	8.519062068	10.18444324	5.19639774	3.633739553	2.887271657	1.661111195	5.651740439	0.209122896	0.260560142
sgPTENhmet02_S3	8.400775673	10.3167431	5.717256773	4.200658724	3.050341301	2.160472369	7.339642886	0.136509187	0.293227649
sgPTENhmet03_S8	8.034056	10.32938615	5.852215751	4.646564378	3.180548916	2.084775443	6.490603136	0.242509616	0.186503862
WT.1_S1.y	8.823230265	10.13588432	2.876962388	3.062304747	2.898870111	1.313437622	5.427838524	0.138853747	0.105902901
WT.2_S7	8.913070121	9.544219856	3.972016647	4.126507526	2.096155275	1.791229179	5.271842511	0.141011677	0.26422307
WT.3_S13	8.691112511	9.381663889	4.076577201	4.270947427	2.503152985	1.624705493	5.353503342	0.131304817	0.100083677
WT.5_S9	8.737719048	9.555811845	3.711911991	4.097008559	2.28639744	1.739627619	5.447557886	0.130299069	0.14745961
WT01_S7	8.81319614	9.878084211	3.450629933	3.934741058	2.802857617	1.561117183	5.770539631	0.239080741	0.088542861

