

Supplementary Materials

Supplementary Materials

Figure S1

Consensus clustering of all HNSCC with k from 2 to 8.

Figure S2

The lactate-related somatic mutations in cluster_A and B. (A) The variants classification, types, SNV class and top mutated genes in HNSCC. (B) The waterfall plot showing the lactate-related genes related to cluster_A in HNSCC. (C) The waterfall plot showing the lactate-related genes related to cluster_B in HNSCC.

Figure S3

Construction the risk model based on LRGS. (A) The LASSO regression to select 10 LRGS to construct a risk model. (B) The ROC analysis evaluating the predictive ability of LRGS from RFS based on clusters when compared to other clinical characteristics. (C) The ROC analysis evaluating the predictive ability of LRGS from RFS based on survival status when compared to other clinical characteristics.

Figure S4

The drug sensitivity and the response to PD1/PD-L1 based on cluster_A and B. (A) The drug sensitivity in cluster_A or B using the OncoPredict algorithm. (B) The response to PD1/PD-L1 in cluster_A or B based on TCIA.

Figure S5

The distribution of immune cell types and immune-related scores from CIBERSORT and ESTIMATE in cluster_A or B.

Figure S6 Unraveling innate mechanism based on cluster_A or B. (A) The volcano plot showing the DEGs based on cluster_A or B. (B) The main pathways from the

GSEA enrichment analysis in comparison of cluster_A or B.

Figure S7 Validation the prognostic ability of hub genes in GEO datasets. (A) The Kaplan-Meier curves of OS for CARS2, NFU1, and SYNJ1 in GSE65858. (B) The Kaplan-Meier curves of OS for CARS2, NFU1, and SYNJ1 in GSE41613. (C) The Kaplan-Meier curves of PFS for CARS2, NFU1, and SYNJ1 in GSE27020. (D) The Kaplan-Meier curves of PFS for CARS2, NFU1, and SYNJ1 in GSE65858.

Figure S8 Validation the prognostic ability of hub genes in IMvigor 210. (A) The Kaplan-Meier curves of OS for CARS2, NFU1, and SYNJ1 in IMvigor 210. (B) The box plot displayed the expression of CARS2, NFU1, and SYNJ1 in diverse overall responses. (C) The box plot displayed the expression of CARS2, NFU1, and SYNJ1 in diverse immune phenotypes.

Figure S9 The relationship between hub genes and important clinical factors. (A) CARS2. (B) NFU1. (C) SYNJ1. (D) The innotation of clinical factors.

Table S1

The gene lists of nine classic lactate metabolism pathways in MSigDB and the two groups of lactate-related genes related to cluster_A and B.

.

Table S2

The coefficient of six crucial genes for calculating LRGS.

Table S3

The coefficient of nine tumor-infiltrating immune-related lncRNAs for calculating TIL_score.

Table S4

The gene lists of prognostic LRGs from Venn plot.

Table S5

The hub gene in HNSCC cells treated with lactate.

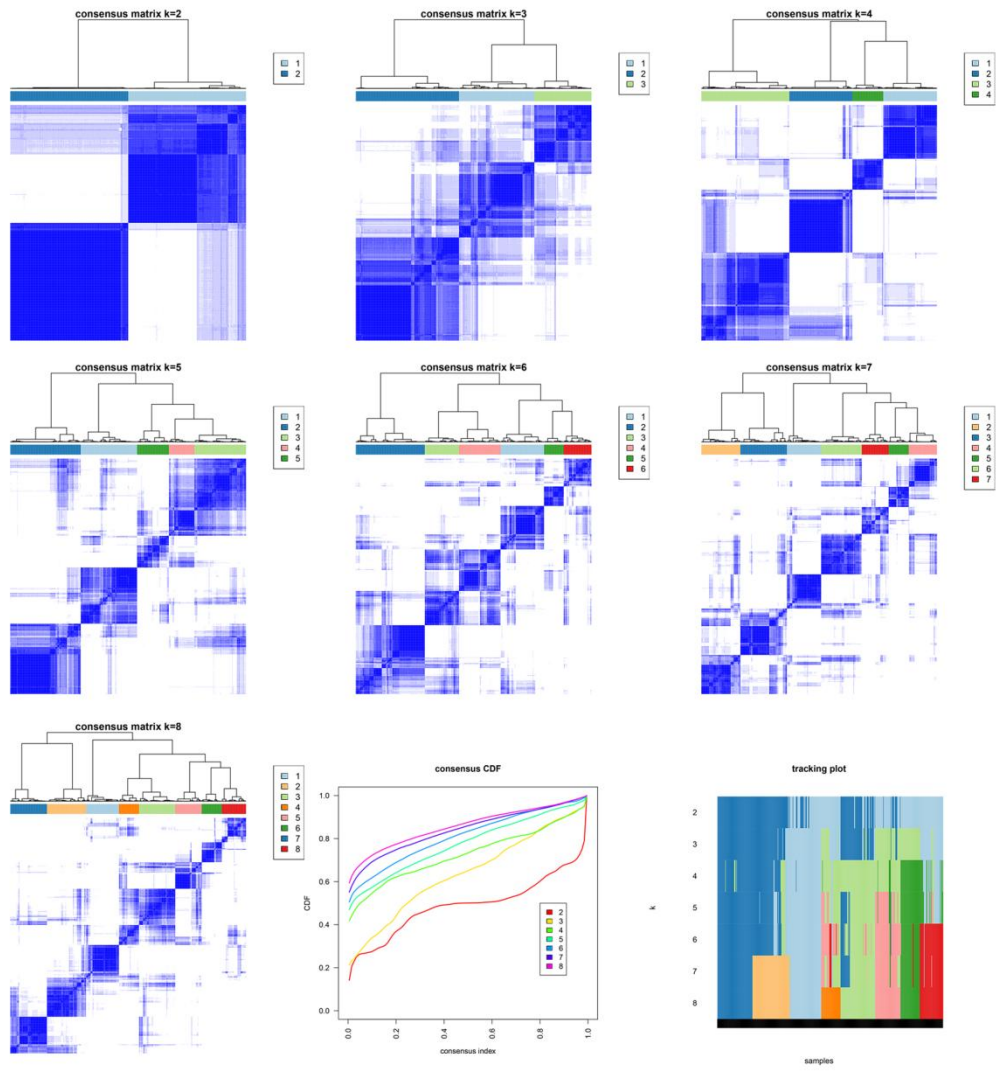


Figure S1

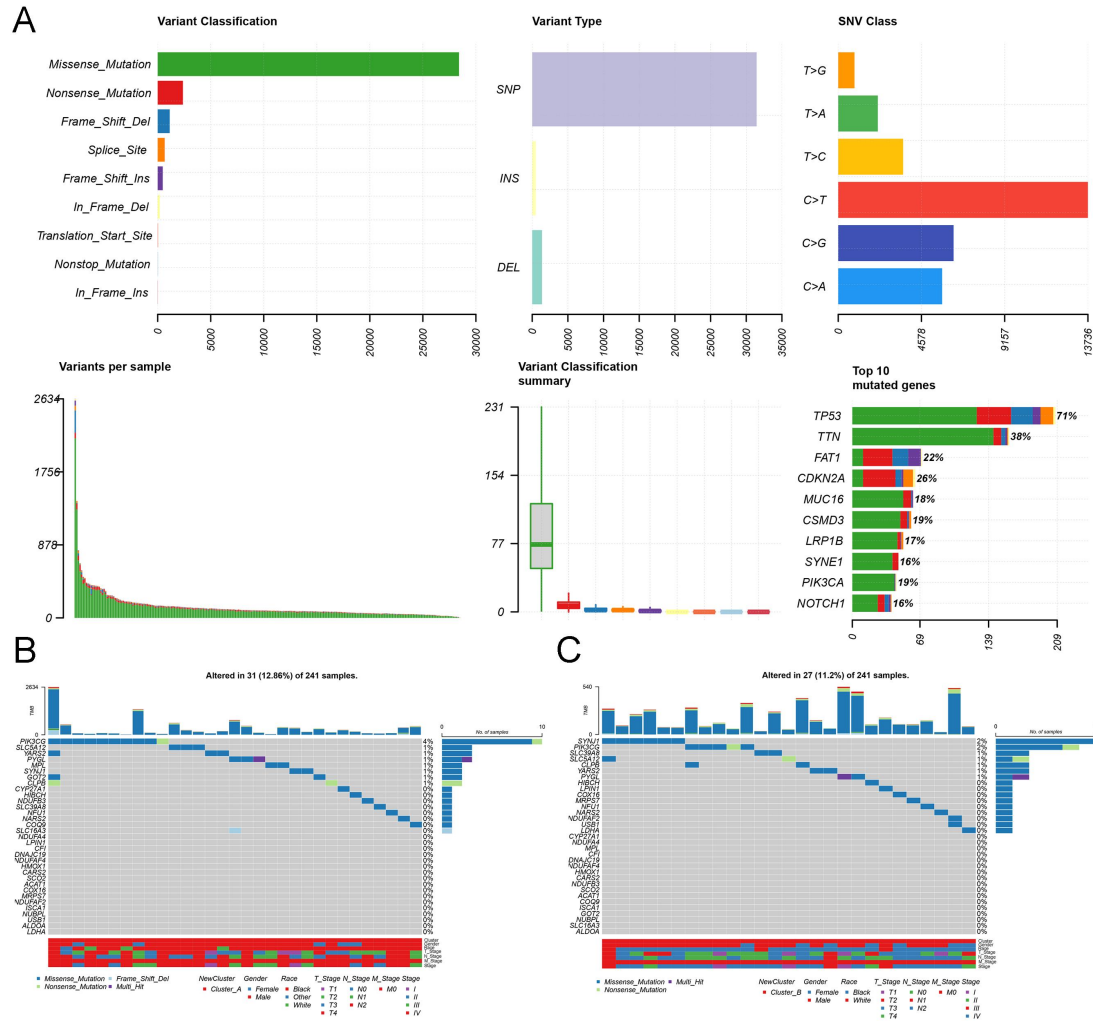


Figure S2

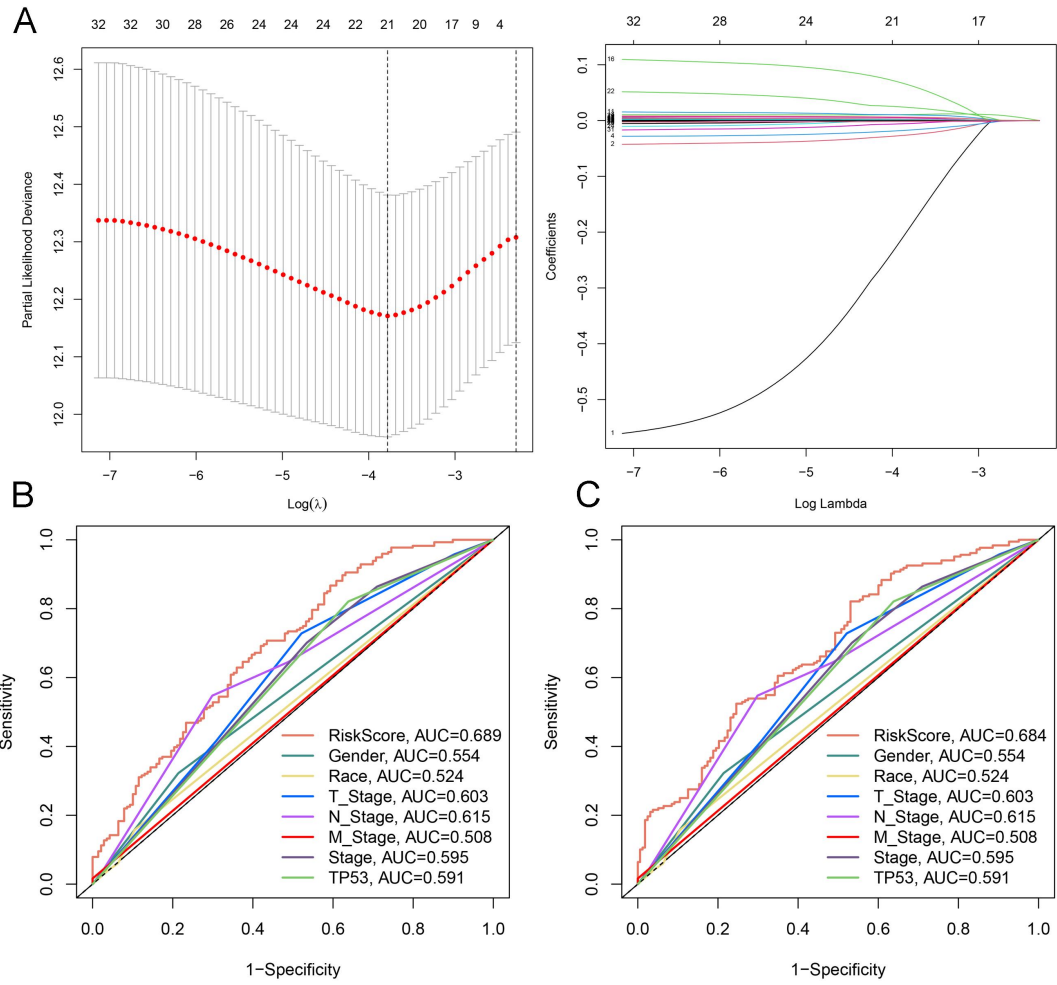


Figure S3

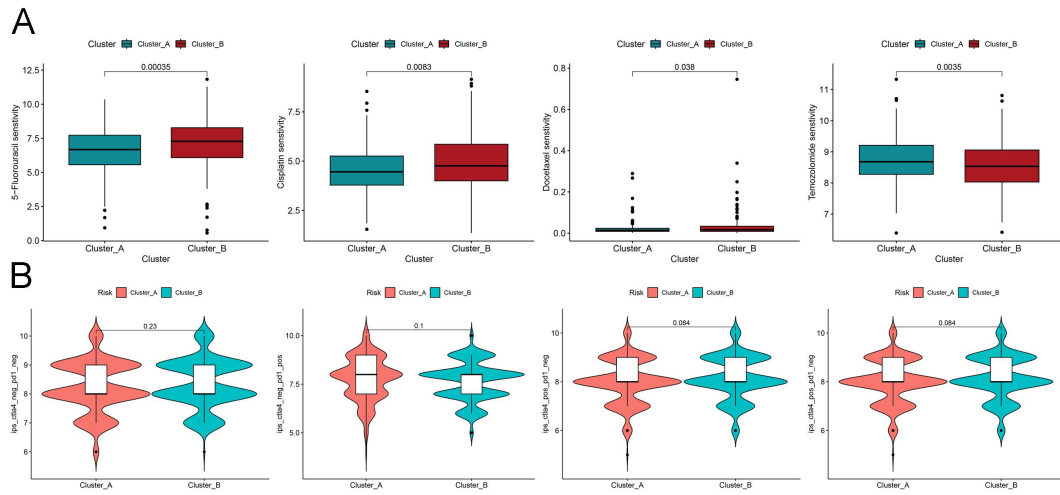


Figure S4

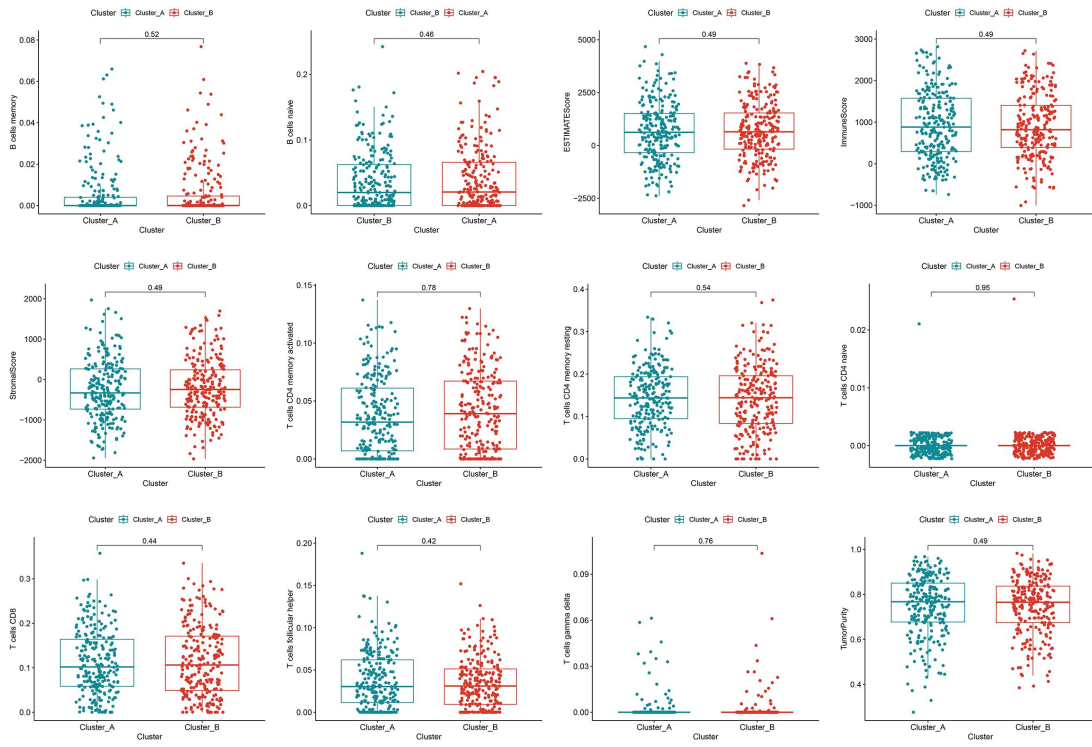


Figure S5

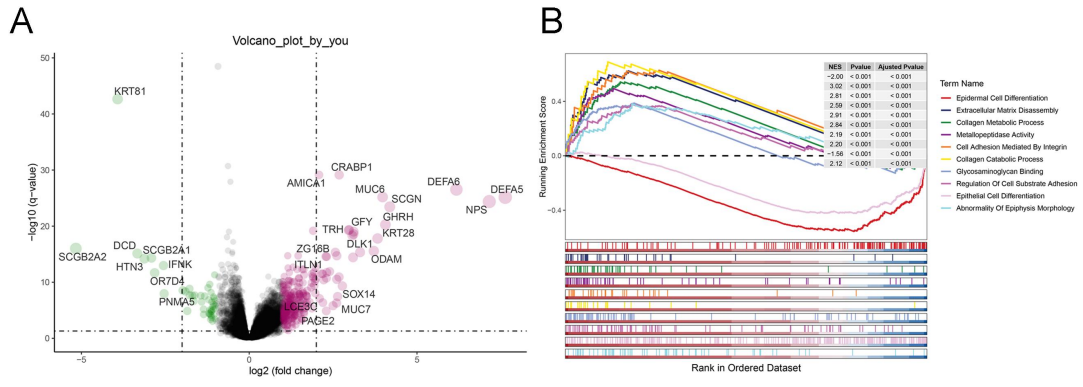


Figure S6

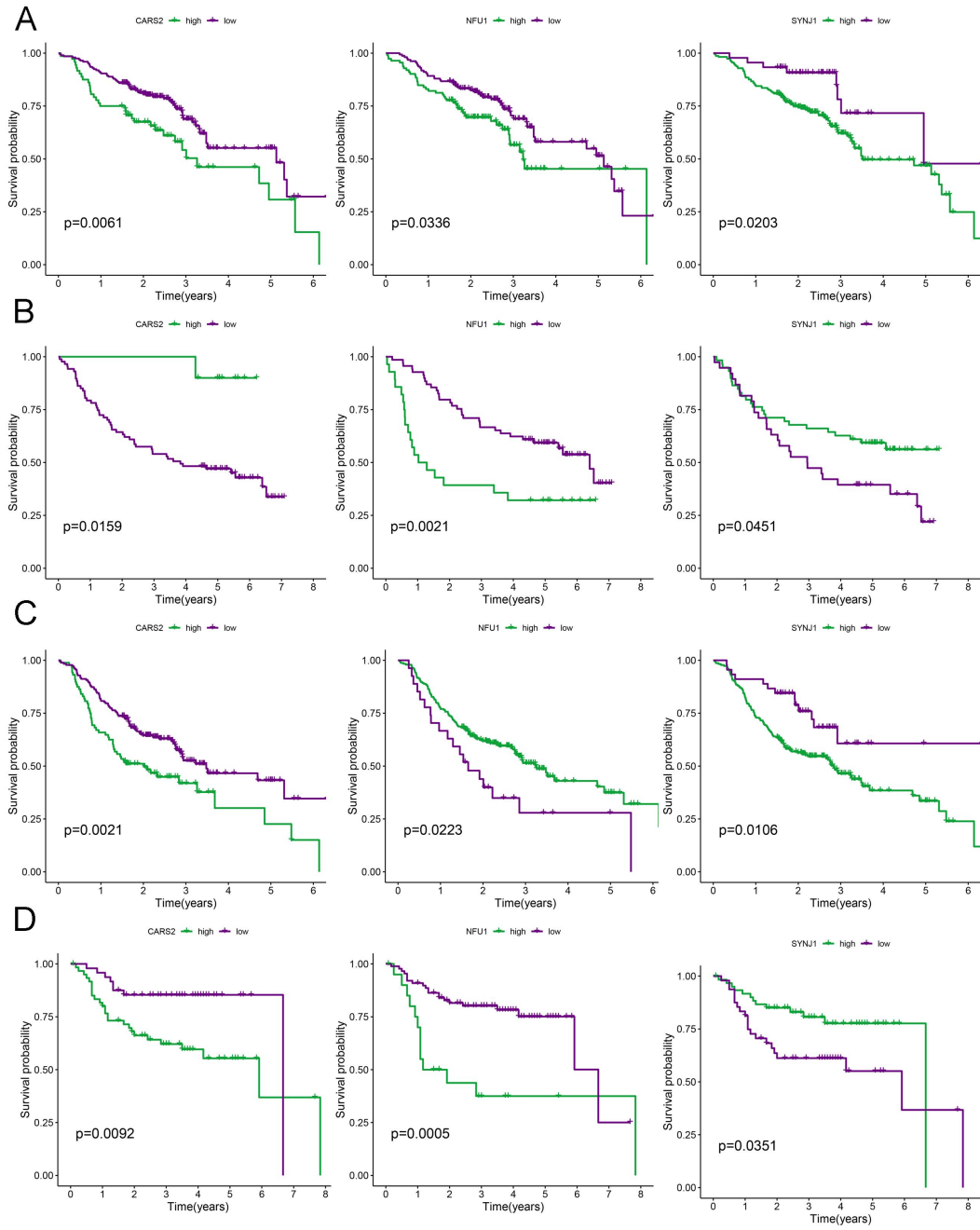


Figure S7

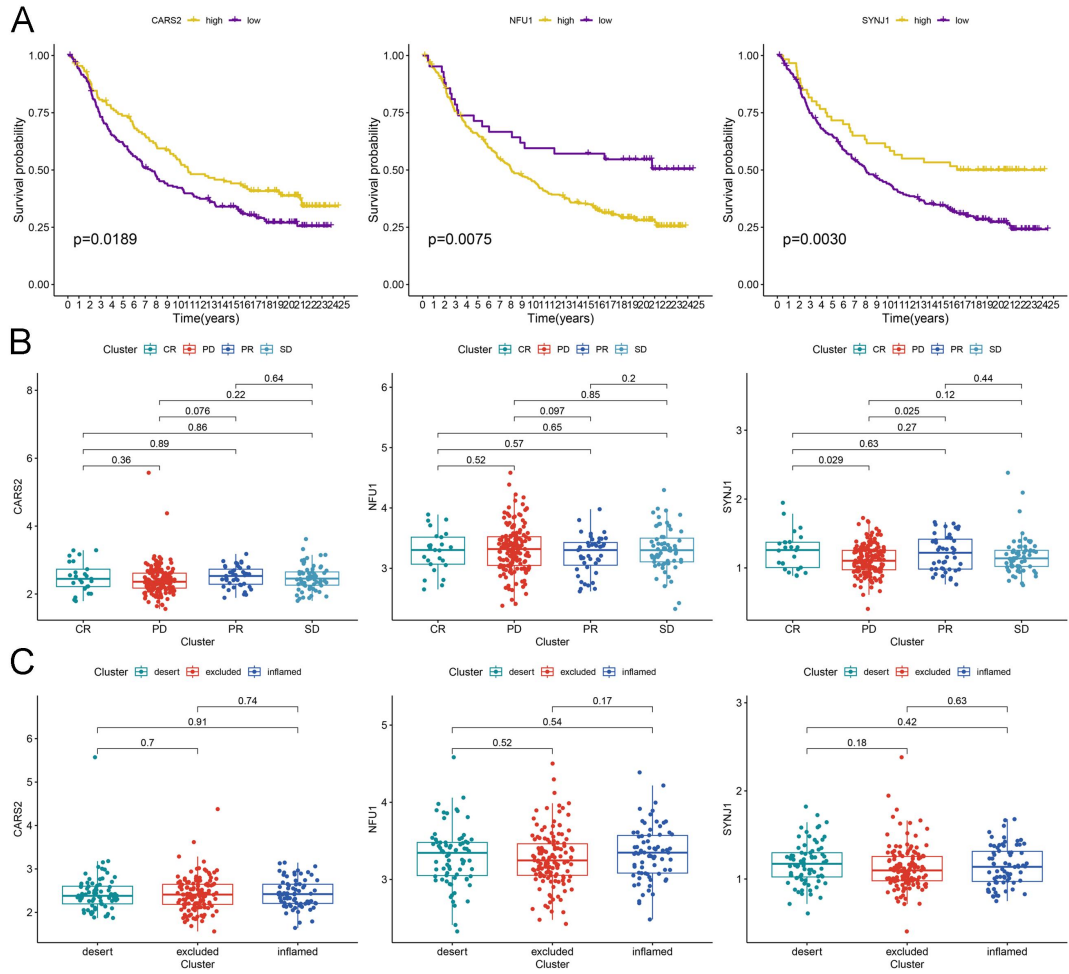


Figure S8

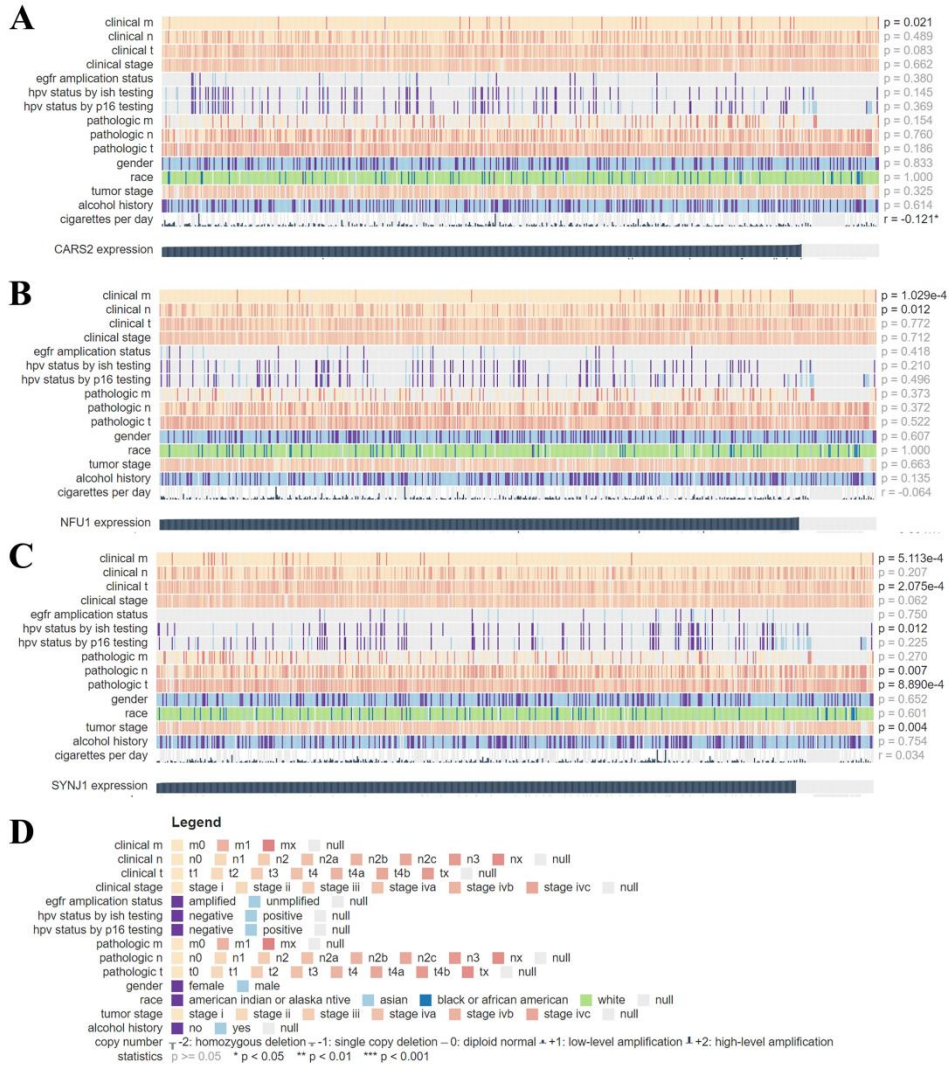


Figure S9

MSigDB from lactate accumulation							Poor OS	Good OS	Cluster_A	Cluster_B
SLC5A12	SUCLG1	INPP5K	LRPPRC	DARS2	COQ2	MRPS14	SLC5A1 2	CYP27A 1	CYP27A 1	SLC39A8
SLC5A8	LYRM7	PIGA	COX20	FOXRED1	GOT2	MRPL44	SLC16A 3	SCO2	NDUFA4	ACAT1
SLC16A8	MTRFR	PIK3CG	MTFMT	TMEM126 B	SLC25A4 2	SOD1	SLC39A 8	FLI1	HIBCH	SLC5A12
SLC16A1	SCO2	PLEC	NDUFA1 1	NDUFA12	MRPS28	STAT2	CFI	LPIN1	LPIN1	COX16
SLC16A3	HELLPAR	TET2	NAXE	COQ8A	TIMM22	C1QBP	IRAK1	MPL	MPL	MRPS7
SLC16A7	SLC25A13	NSUN2	COX4I1	RARS2	GYS2	TK2	USB1	PIK3CG	PIK3CG	NFU1
LDHAL6 A	TCIRG1	POMGNT 1	COX6B1	SLC25A19	HMGCL	TUFM	COX20	PLA2G6	SYNJ1	NARS2
LDHD	RXYLT1	PNPLA2	COX8A	SLC13A3	ACAT1	UQCRB	COX15	SYNJ1	CFI	COQ9
LDHA	PITRM1	ZNFX1	COX10	SLC2A1	LIPT2	UQCRC2	NFU1		DNAJC1 9	NDUFAF 2
LDHB	POMT1	RB1	COX15	NDUFAF5	ACAT2	UQCRH	NDUFA 4		NDUFAF 4	ISCA1
LDHAL6 B	KLF1	RHAG	TXN2	NARS2	LETM1	CA5A	DARS2		HMOX1	GOT2
DNM1L	B4GAT1	RHCE	TPK1	NUBPL	CHCHD1 0	UQCC3	RARS2		CARS2	NUBPL
FARS2	CHEK2	RHD	NFU1	PDHX	MIPEP	CARS2	SLC13A 3		NDUFB3	CLPB
NDUFAF 6	LYST	RPS14	NDUFAF 8	SLC19A3	ALDH6A 1	PPCS	NARS2		SCO2	YARS2
CYP27A1	COL4A1	ABCG8	NDUFAF 4	CLPB	MT-TI	TTC26	NUBPL			USB1
ECHS1	CPT2	SIL1	SLC25A4	UQCC2	MT-TL2	TARS2	CLPB			PYGL
NDUFAF 3	CDAN1	SLC4A1	NDUFS7	COA8	MT-TP	PUS1	AIFM1			SLC16A3
HTRA2	B3GALNT 2	SLC19A1	MECP2	GFM2	NDUFC2	ISCA1	DNAJC1 9			ALDOA
HSD17B1 0	DAG1	SPP1	MPV17	COX14	OGDH	GTPBP3	GOT2			LDHA
KARS1	FKTN	AKR1D1	MT-ATP6	ALDH4A1	PNPLA8	SERAC1	ACAT1			
MT-CO1	ALDOA	STAT4	MT-ND2	PNPT1	PC	YARS1	YARS2			
MT-CO2	FLI1	TP53	MT-ND3	AIFM1	MRPS16	SLC25A1 2	COQ9			
MT-CO3	LPIN1	CRPPA	MT-TK	ATPAF2	YARS2	SYNJ1	PYGL			
MT-ND1	VPS13A	XK	MT-TN	NDUFAF2	MRPS7	HS6ST2	CARS2			

MT-ND4	GAA	FKRP	MT-TV	TIMM50	MRPS2	NFS1	TARS2
MT-ND5	GATA1	USB1	NDUFA1	LONP1	COQ4	COX5A	ISCA1
MT-ND6	GATA2	CALR	NDUFA2	WARS2	MPC1	PMPCB	
MT-TF	CBLIF	PLA2G6	NDUFA4	LIAS	UPB1		
MT-TH	ACAD9	POMK	NDUFA6	ADAMTS1 3	SLC25A3		
MT-TL1	POMT2	POMGNT 2	NDUFA8	PLPBP	PHKG2		
MT-TQ	HBB	CAV3	NDUFA1 0	POLG2	POLG		
MT-TS2	CFH	MLIP	NDUFB3	FDX2	PDP1		
MT-TW	HLA-DRB 1	SLC7A7	NDUFB9	SLC25A26	TMEM70		
NDUFB7	HMGCS2	LARGE1	NDUFS1	SFXN4	PNPO		
NDUFB8	HMOX1	KIF23	NDUFS3	EARS2	ATAD3A		
NDUFS2	KY	PIEZO1	NDUFV1	MICOS13	TRMU		
MECR	ACADM	TSMF	NDUFS6	TANGO2	NAXD		
COX16	CFI	MRPL3	NDUFS8	DNAJC19	AGK		
POLRMT	IRAK1	CYC1	NDUFV2	COX6A2	NGLY1		
LYRM4	JAK2	PDSS1	RRM2B	SLC25A10	TWNK		
VAR52	KCNN4	MDH2	NDUFA1 3	DGUOK	MRPS22		
SQOR	LIPA	NDUFA9	NDUFAF 1	DLD	COQ9		
SDHB	CD46	NDUFB1 0	TRAPPC1 2	DTYMK	PDSS2		
SLC39A8	MPL	NDUFS4	TACO1	FASTKD2	AARS2		
MRPS34	MTHFD1	BCS1L	TIMMDC 1	ISCU	TRMT5		
SURF1	MVK	SDHA	PDHA1	RNASEH1	PYGL		
COG8	MYC	GFM1	LIPT1	MTO1	RARS1		
HPDL	OCRL	PRORP	NDUFB1 1	FBXL4	MRPL12		
SUCLG1	INPP5K	PET100	TRMT10 C	HIBCH	SCO1		
LYRM7	PIGA	PET117	RMND1	UQCRQ	NSUN3		

Table S1

Gene	Coef
MPL	-0.187781556
LPIN1	-0.025384765
NFU1	0.010898831
HIBCH	-0.016822569
NDUFB3	0.000769955
CYP27A1	-0.001611948
SLC39A8	0.001117786
CFI	0.004975383
NDUFAF4	0.010080619
SLC5A12	0.062473431
ACAT1	0.004607103
CARS2	0.006013107
NUBPL	0.023182463
PYGL	0.000547012
ALDOA	0.000339325
USB1	0.002425176
GOT2	0.000639595
SLC16A3	0.001605662
SYNJ1	-0.005200659
HMOX1	0.000225916
SCO2	-0.001516521

Table S2

id	coef	HR	HR.95L	HR.95H	pvalue
ITPKB-IT1	-0.16100272 2	0.85128975 4	0.76530191 6	0.94693901 9	0.00304164 7
SNHG15	-0.04926652 5	0.95192738 3	0.91031167 7	0.99544558 8	0.03076415
PCOLCE-AS1	-0.06088019 3	0.94093596 4	0.87982290 9	1.00629397 1	0.07559385 5
SNHG6	0.039824613	1.04062824 6	0.99627989 6	1.08695071 6	0.07309530 1
WAC-AS1	-0.06043872 2	0.94135145 1	0.89747141	0.98737691 8	0.01308107 8
TMEM254-AS1	0.038920191	1.03968750 4	0.99133512 8	1.09039826 7	0.10920013 2
NUTM2A-AS1	0.047952284	1.04912059 4	0.99890614 5	1.10185929 5	0.05533603 5
VPS9D1-AS1	0.044099557	1.04508639 5	1.00058365 1	1.09156847 8	0.04700624
ITGB2-AS1	-0.04985878 7	0.95136376	0.90628793 8	0.99868150 7	0.04408956 8

Table S3

TCGA	GSE65858	GSE41613	GSE27070 PFS	GSE65858 PFS
MPL	GOT2	NUBPL	NFU1	SLC16A3
LPIN1	SLC16A3	USB1	LPIN1	HIBCH
NFU1	ACAT1	HIBCH	SCO2	HMOX1
HIBCH	CARS2	NFU1	CARS2	CARS2
NDUFB3	HMOX1	ACAT1	NDUFAF4	GOT2
CYP27A1	ALDOA	NDUFB3	NUBPL	CFI
SLC39A8	MPL	SCO2	SYNJ1	LPIN1
CFI	HIBCH	MPL	GOT2	ACAT1
NDUFAF4	SYNJ1	CARS2	MPL	SYNJ1
SLC5A12	NFU1	SLC39A8		NFU1
ACAT1	NDUFB3	PYGL		SLC39A8
CARS2		ALDOA		ALDOA
NUBPL		SLC5A12		
PYGL		SYNJ1		
ALDOA		HMOX1		
USB1				
GOT2				
SLC16A3				
SYNJ1				
HMOX1				
SCO2				

Table S4

gene_name	logFC	AveExpr	t	P.Value	adj.P.Val	B
CARS2	-2.492630409	9.143093418	-17.58409655	1.80E-05	0.000896265	3.55075874
SYNJ1	0.33924216	1.0002662	5.393943076	0.003556666	0.019718563	-2.708848056
NFU1	1.499525671	17.18755313	2.422781145	0.063069709	0.169208894	-6.014724051

Table S5