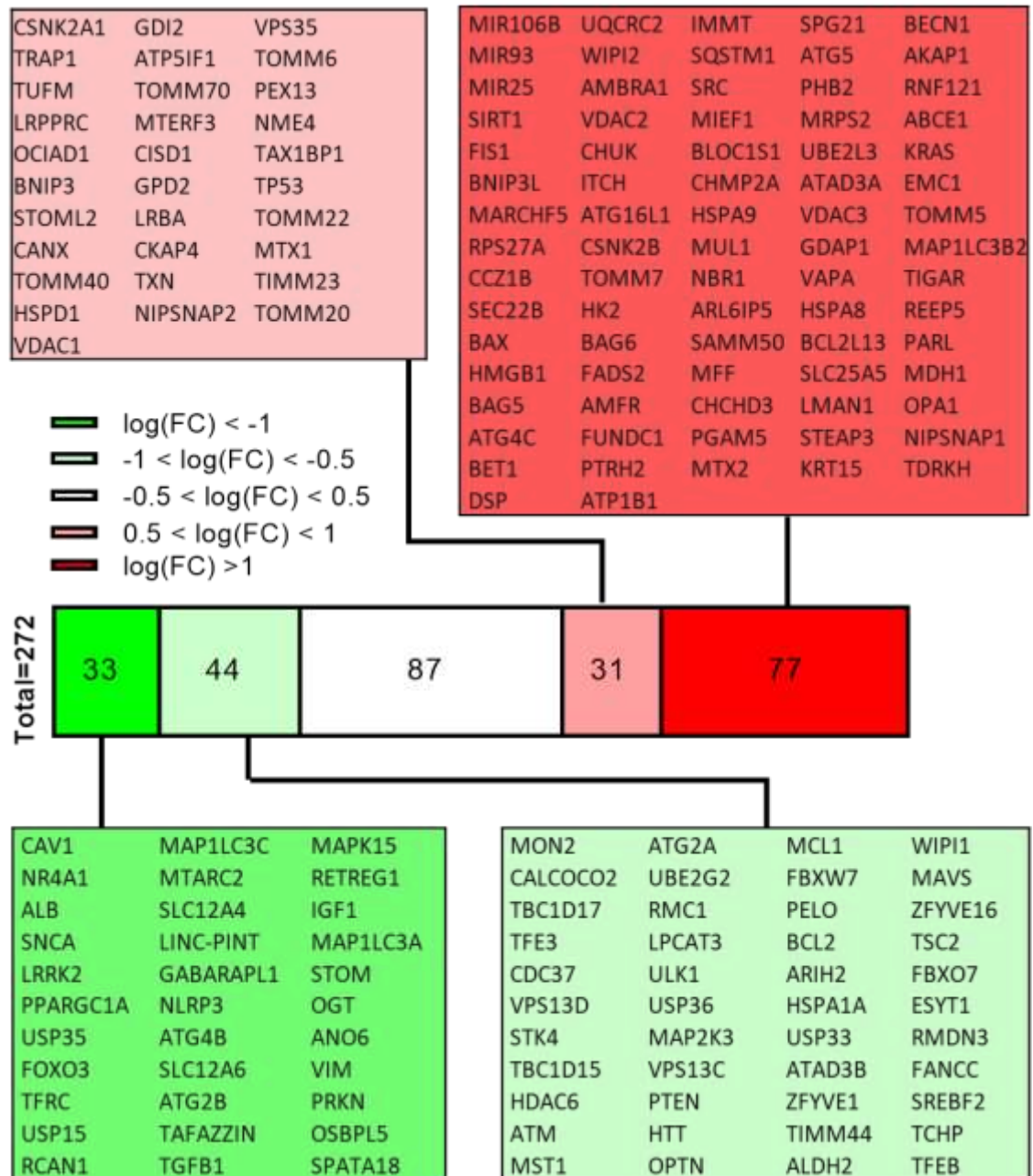**Table S1.** The mitophagy related genes extracted from GeneCards database classified by the relevance score

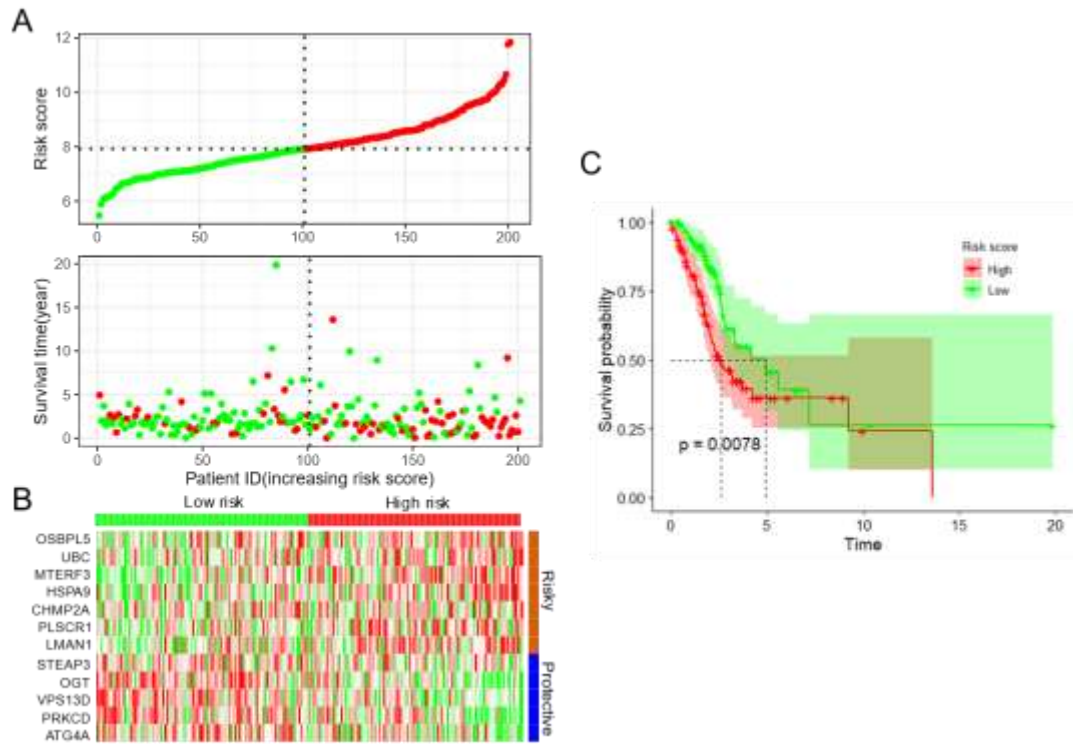| Relevance score	Count	Gene symbol
> 5	15	PRKN PINK1 MAP1LC3B VDAC1 FUNDC1 MFN2 SQSTM1 MAP1LC3A PHB2 ATG13 AMBRA1 ULK1 UBC TOMM20 USP30
4-5	10	CLEC16A DNM1L RIMOC1 UBA52 MFN1 OPTN HUWE1 PGAM5 SLC25A4 RNF41
3-4	29	ATG7 UBB SLC25A5 VPS13D TOMM40 VPS13C ATG4D TAFAZZIN ATG4B USP15 GABARAPL2 TOMM7 BNIP3L BECN1 ABCE1 CERS1 ATG5 TOMM70 BNIP3 TIGAR RHOT1 RPS27A LRBA ARFIP2 TOMM22 PHB1 FBXO7 RAB7A SPATA33
2-3	37	MAP1LC3B2 MUL1 GABARAP CHUK ATG9A TP53 CISD1 FKBP8 CALCOCO2 CNOT4 CSNK2A1 TBK1 VDAC2 CSNK2A2 MTX1 ATG4A BCL2L13 SNCA MON1A PELO HDAC6 LRRK2 PRKAA1 MTARC2 PTRH2 BCL2L1 FIS1 OPA1 ATG14 TDRKH GBA1 ATG12 UBE2L3 MFF MAP1LC3C PI4KB SIRT1
1-2	181	WIPI1 VCP NBR1 SPATA18 HTRA2 SESN2 ATG4C SAMM50 IMMT MAPK14 FANCC TBC1D5 STX10 STK4 NLRP3 ATAD3A MARCHF5 PLSCR1 BCL2 SRC CSNK2B TOMM5 MTERF3 TOMM6 MIEF1 BAG5 PEX13 MTX2 HSPA8 OGT RETREG1 MAVS PTEN CHCHD3 GABARAPL1 PARL TSC2 VDAC3 HK2 MAPK1 TSPO MAP2K1 FOXO3 MDH1 TBC1D15 OCIAD1 USP8 PI4K2A STOM KRT15 BLOC1S1 HIF1A ATM LRPPRC ATP1B1 APP BCAS3 PHAF1 ZFYVE16 BET1 GDAP1 WDR26 MCL1 LINC-PINT NR4A1 ALB HSPD1 HTT ATG16L1 TFEB NIPSNAP1 BAG6 CDC37 SIRT3 MST1 TRAP1 ATG2B TGFB1 NFE2L2 UQCRC2 NIPSNAP2 TFE3 VAPA DSP CAV1 TOM1 NME4 USP36 UBXN1 RMC1 RNF31 TCHP MTOR GPD2 SHC1 USP33 STX17 RNF121 CANX EPHA2 SLC12A6 ITCH SLC12A4 STEAP3 FADS2 UBE2G2 VPS35 ANO6 EMC1 LPCAT3 ARL6IP5 MON2 AMFR AKAP1 REEP5 SNX3 GDI2 CHMP2A ESYT1 ATG2A SPG21 RMDN3 SEC22B ARMCX3 TBC1D17 CCZ1B FLOT2 SH3GLB1 SREBF2 MIR155 PPARGC1A ALDH2 HSPA1L HMGB1 MAP2K3 LMAN1 FBXW7 ARIH2

ATP5IF1	MAP2K2	TIMM23	UBXN6	FTMT	HSPA9
WIPI2	ZFYVE1	TIMM44	HRAS	TFRC	NDUFA10
NRF1	KRAS	PRKAA2	AKT1	RCAN1	RB1CC1
USP35	TUFM	PRPF8	BAX	MAPK15	VIM
MIR106B	MIR93	MIR25	HK1	IGF1	NDUFV1
OSBPL5	RDH13	TAX1BP1	CKAP4	MRPS2	PRKCD
BIRC2	HSPA1A	TXN	HNRNPM	STOML2	ATAD3B
LOC105378097					
Total		**272**			

Table S2. Analysis of the difference of mitophagy risk score in different clinic-pathological features

Pathological	N	Risk score	PValue
Gender			
female	270	7.904±1.107	
male	234	8.058±1.04	0.152
Age			
> 60	336	7.919±1.096	
≤ 60	158	8.107±1.026	0.069
Distant metastasis			
M0	335	8.025±1.126	
M1	25	8.441±1.341	0.082
Lymph node metastasis			
N0	324	7.841±1.04	
N1	95	8.166±1.036	0.052
N2	71	8.399±1.125	**0.001**
N3	2	8.035±0.798	0.995
Invasion depth			
T1	169	7.72±0.919	
T2	269	8.04±1.053	**0.011**
T3	45	8.287±1.392	**0.007**
T4	18	8.489±1.428	**0.019**
Stage			
Stage I	270	7.765±0.991	
Stage II	120	8.075±1.07	0.056
Stage III	80	8.454±1.107	**<0.001**
Stage IV	26	8.432±1.315	**0.014**
Smoking history			
Current	119	8.108±0.99	
Never	72	7.711±1.105	**0.034**
Reformed (≤15)	128	7.705±1.091	0.985
Reformed (>15)	167	8.164±1.085	**0.015**

CSNK2A1	GDI2	VPS35
TRAP1	ATP5IF1	TOMM6
TUFM	TOMM70	PEX13
LRPPRC	MTERF3	NME4
OCIAD1	CISD1	TAX1BP1
BNIP3	GPD2	TP53
STOML2	LRBA	TOMM22
CANX	CKAP4	MTX1
TOMM40	TXN	TIMM23
HSPD1	NIPSNAP2	TOMM20
VDAC1		

MIR106B	UQCRC2	IMMT	SPG21	BECN1
MIR93	WIPI2	SQSTM1	ATG5	AKAP1
MIR25	AMBRA1	SRC	PHB2	RNF121
SIRT1	VDAC2	MIEF1	MRPS2	ABCE1
FIS1	CHUK	BLOC1S1	UBE2L3	KRAS
BNIP3L	ITCH	CHMP2A	ATAD3A	EMC1
MARCHF5	ATG16L1	HSPA9	VDAC3	TOMM5
RPS27A	CSNK2B	MUL1	GDAP1	MAP1LC3B2
CCZ1B	TOMM7	NBR1	VAPA	TIGAR
SEC22B	HK2	ARL6IP5	HSPA8	REEP5
BAX	BAG6	SAMM50	BCL2L13	PARL
HMGB1	FADS2	MFF	SLC25A5	MDH1
BAG5	AMFR	CHCHD3	LMAN1	OPA1
ATG4C	FUNDC1	PGAM5	STEAP3	NIPSNAP1
BET1	PTRH2	MTX2	KRT15	TDRKH
DSP	ATP1B1			

Legend:
- log(FC) < -1
- -1 < log(FC) < -0.5
- -0.5 < log(FC) < 0.5
- 0.5 < log(FC) < 1
- log(FC) >1

Total=272

33	44	87	31	77

CAV1	MAP1LC3C	MAPK15
NR4A1	MTARC2	RETREG1
ALB	SLC12A4	IGF1
SNCA	LINC-PINT	MAP1LC3A
LRRK2	GABARAPL1	STOM
PPARGC1A	NLRP3	OGT
USP35	ATG4B	ANO6
FOXO3	SLC12A6	VIM
TFRC	ATG2B	PRKN
USP15	TAFAZZIN	OSBPL5
RCAN1	TGFB1	SPATA18

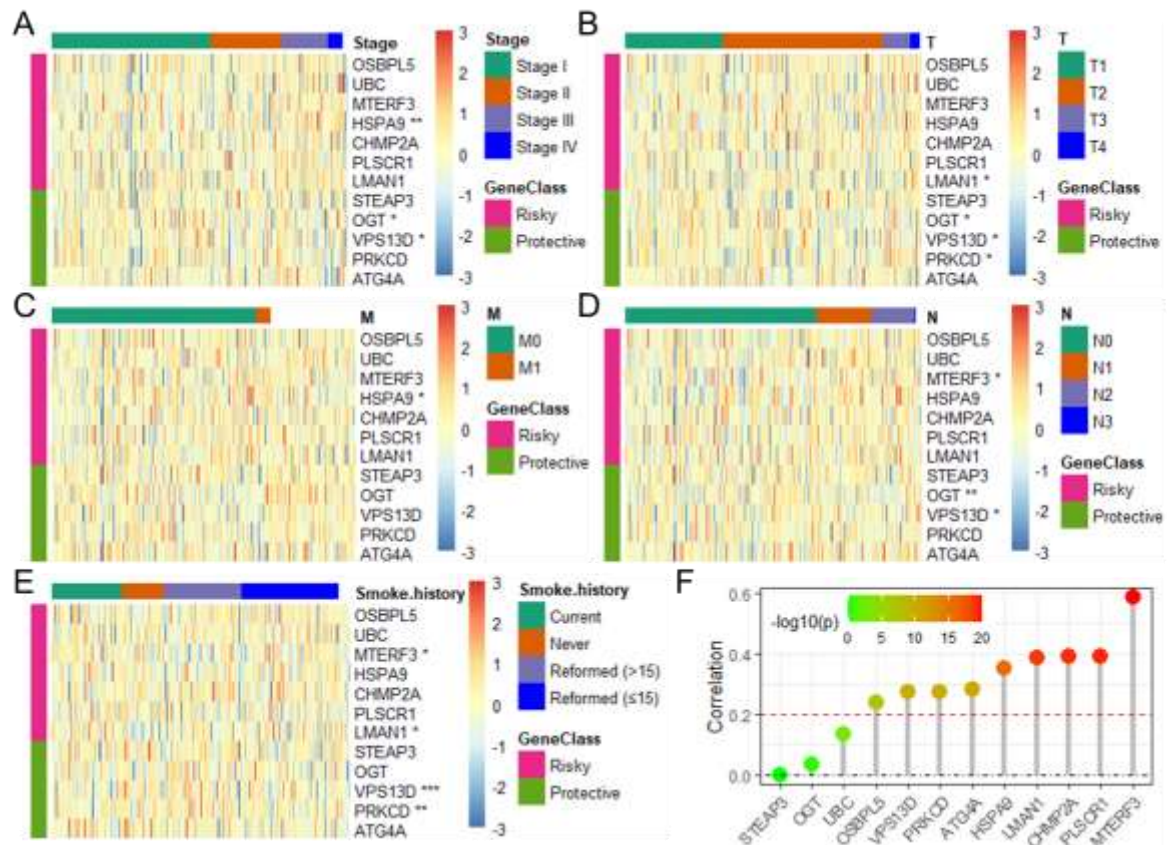| MON2	ATG2A	MCL1	WIPI1
CALCOCO2	UBE2G2	FBXW7	MAVS
TBC1D17	RMC1	PELO	ZFYVE16
TFE3	LPCAT3	BCL2	TSC2
CDC37	ULK1	ARIH2	FBXO7
VPS13D	USP36	HSPA1A	ESYT1
STK4	MAP2K3	USP33	RMDN3
TBC1D15	VPS13C	ATAD3B	FANCC
HDAC6	PTEN	ZFYVE1	SREBF2
ATM	HTT	TIMM44	TCHP
MST1	OPTN	ALDH2	TFEB

Figure S1. Different expression analysis of 272 MRGs in TCGA LUAD dataset.

Figure S2. Validation of the prognostic model with 12 MRGs in internal testing set. (A) Risk score distribution and survival status of training group. (B) Heatmap shows the expression of 12 MRGs in training group. (C) Kaplan–Meier curve of overall survival in training group. MRGs: mitophagy-related genes.
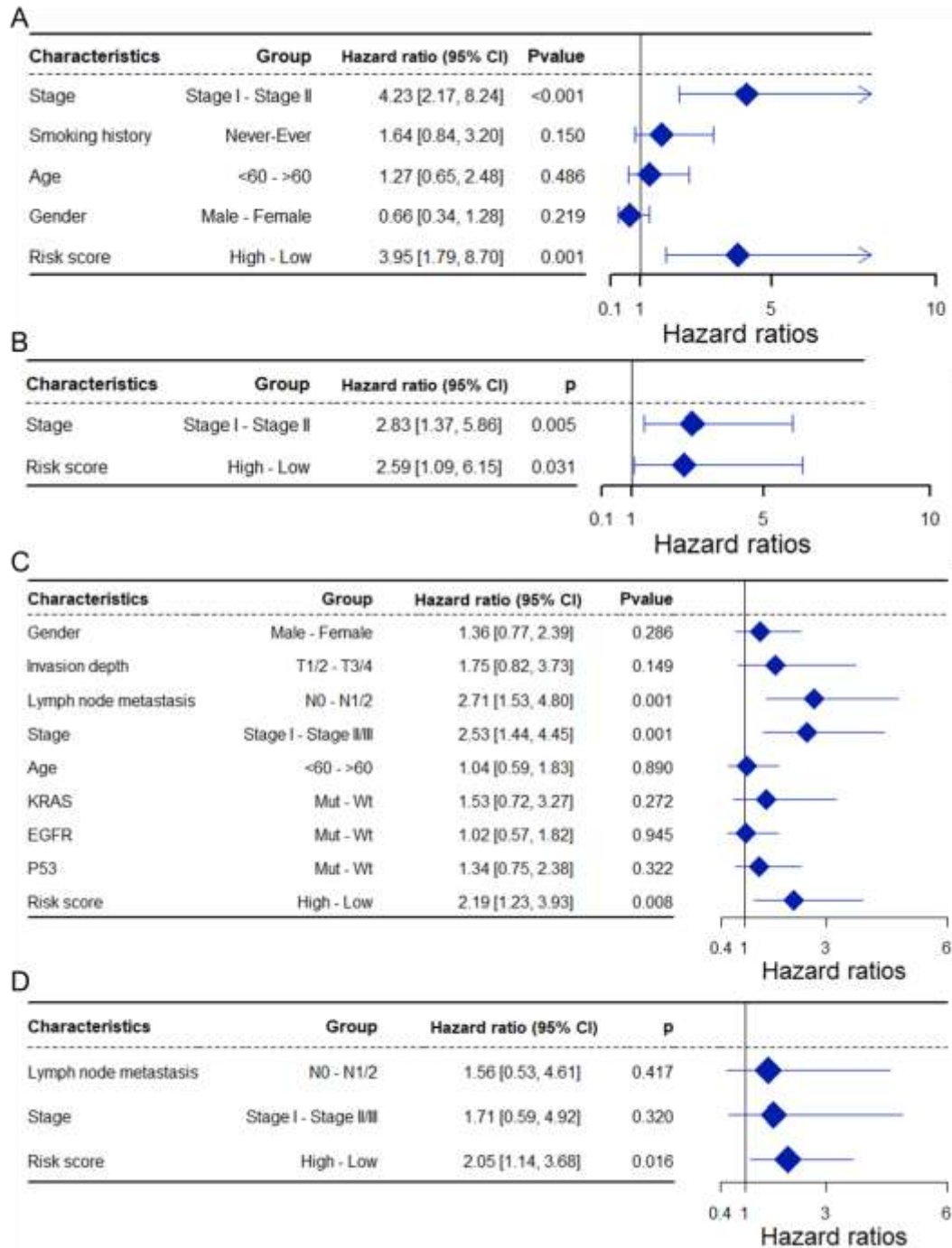
Figure S3. Kaplan–Meier curve of mitophagy risk score for different survival indicators. Kaplan–Meier curve of mitophagy risk score for DSS in training set (A) and entire TCGA-LUAD (B) dataset. Kaplan–Meier curve of mitophagy risk score for DFI in training set (C) and entire TCGA-LUAD (D) dataset. Kaplan–Meier curve of mitophagy risk score for PFI in training set (E) and entire TCGA-LUAD (F) dataset. DSS: disease specific survival; DFI: disease free interval; PFI: progression free interval.
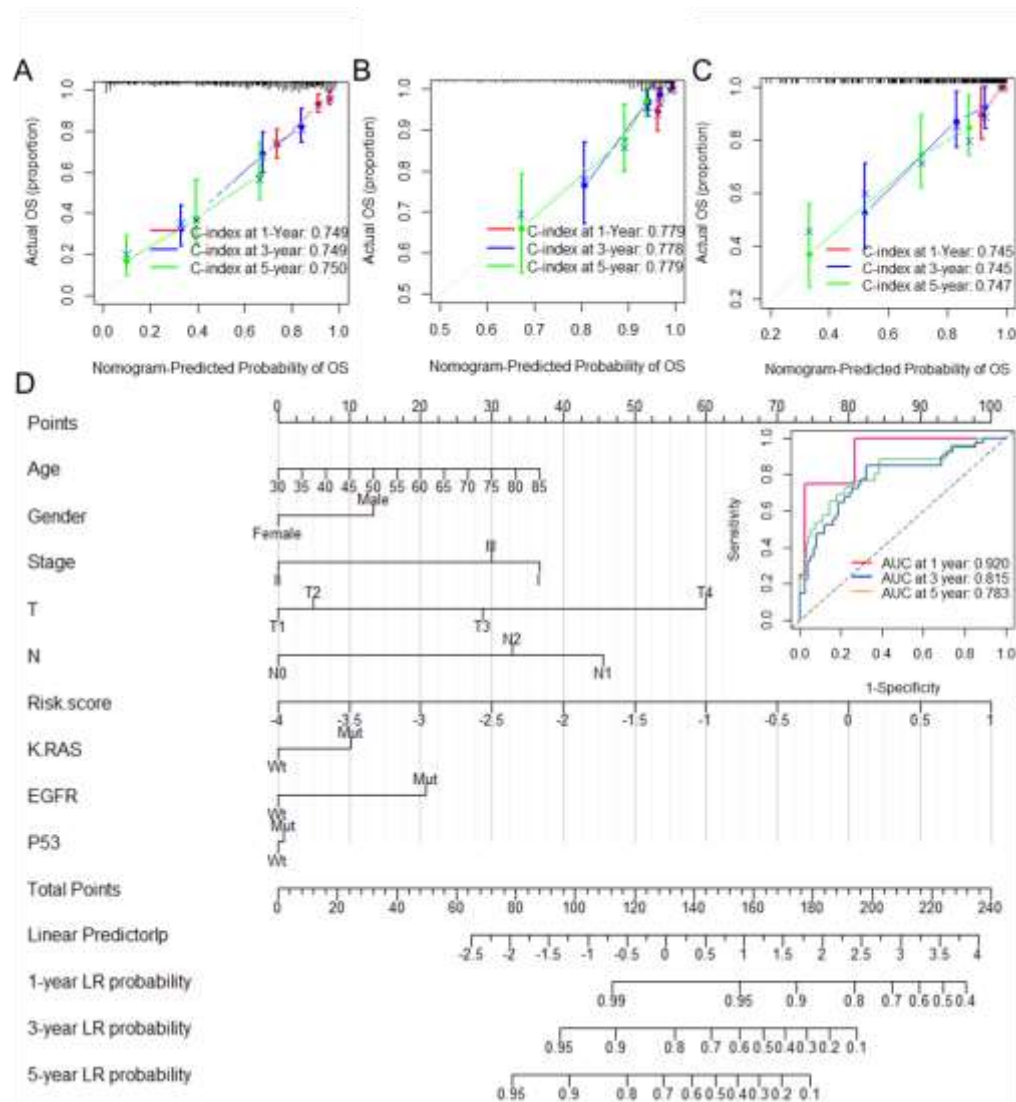
Figure S4. Expression of the 12 MRGs in TCGA-LUAD samples with different pathological features. Expression of the 12 MRGs in TCGA-LUAD samples with different stages (A), invasion depth (B), distant metastasis (C), lymph node metastasis (D), and smoking history. (F) correlation analysis between mitophagy risk score and the expression of 12 MRGs. TCGA: The Cancer Genome Atlas; LUAD: lung adenocarcinoma; MRGs: mitophagy related genes.

A

Characteristics	Group	Hazard ratio (95% CI)	Pvalue
Stage	Stage I - Stage II	4.23 [2.17, 8.24]	<0.001
Smoking history	Never-Ever	1.64 [0.84, 3.20]	0.150
Age	<60 - >60	1.27 [0.65, 2.48]	0.486
Gender	Male - Female	0.66 [0.34, 1.28]	0.219
Risk score	High - Low	3.95 [1.79, 8.70]	0.001

B

Characteristics	Group	Hazard ratio (95% CI)	p
Stage	Stage I - Stage II	2.83 [1.37, 5.86]	0.005
Risk score	High - Low	2.59 [1.09, 6.15]	0.031

C

Characteristics	Group	Hazard ratio (95% CI)	Pvalue
Gender	Male - Female	1.36 [0.77, 2.39]	0.286
Invasion depth	T1/2 - T3/4	1.75 [0.82, 3.73]	0.149
Lymph node metastasis	N0 - N1/2	2.71 [1.53, 4.80]	0.001
Stage	Stage I - Stage II/III	2.53 [1.44, 4.45]	0.001
Age	<60 - >60	1.04 [0.59, 1.83]	0.890
KRAS	Mut - Wt	1.53 [0.72, 3.27]	0.272
EGFR	Mut - Wt	1.02 [0.57, 1.82]	0.945
P53	Mut - Wt	1.34 [0.75, 2.38]	0.322
Risk score	High - Low	2.19 [1.23, 3.93]	0.008

D

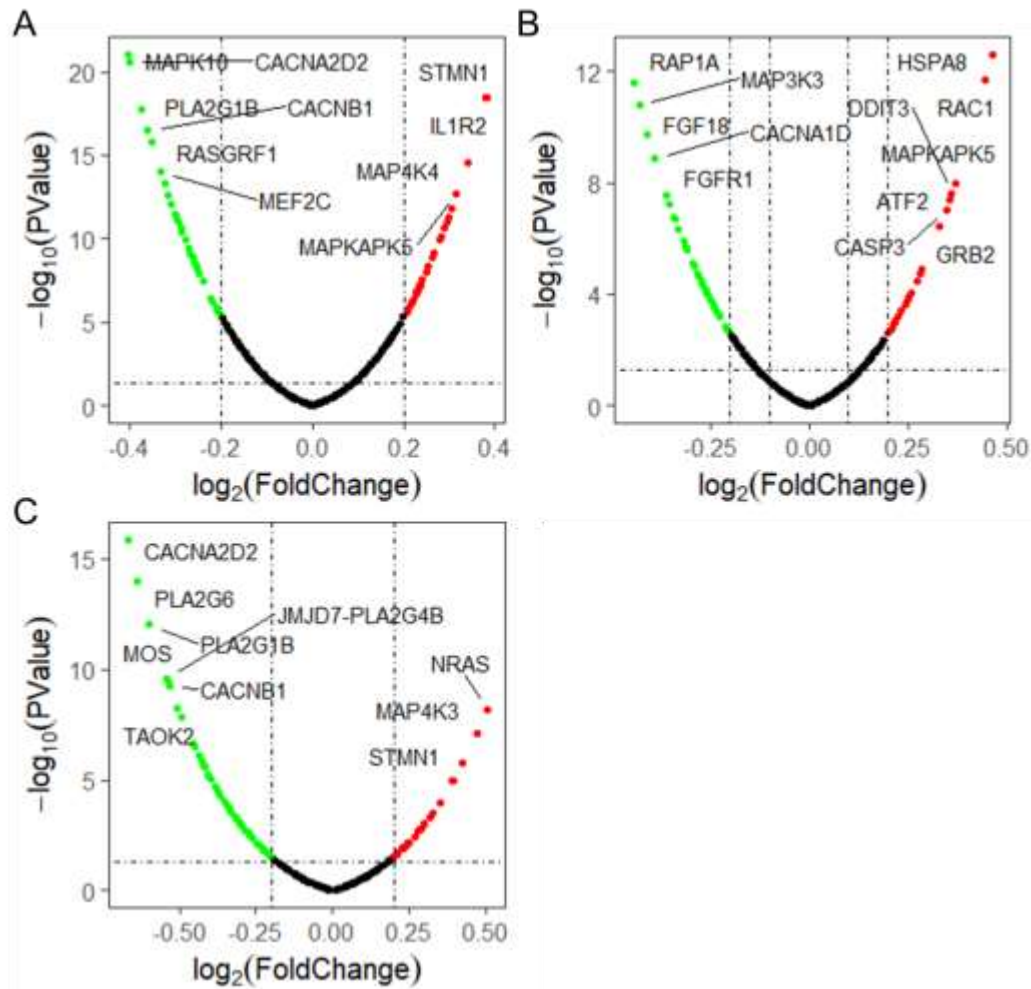| Characteristics	Group	Hazard ratio (95% CI)	p
Lymph node metastasis	N0 - N1/2	1.56 [0.53, 4.61]	0.417
Stage	Stage I - Stage II/III	1.71 [0.59, 4.92]	0.320
Risk score	High - Low	2.05 [1.14, 3.68]	0.016

Figure S5. Mitophagy risk score is an independent prognostic factor for overall survival in validation datasets. Univariate (A) and multivariate (B) Cox regression analyses of risk score and clinic-pathological features for overall survival in GSE31210 dataset. Univariate (A) and multivariate (B) Cox regression analyses of risk score and clinic-pathological features for overall survival in GSE13213 dataset.
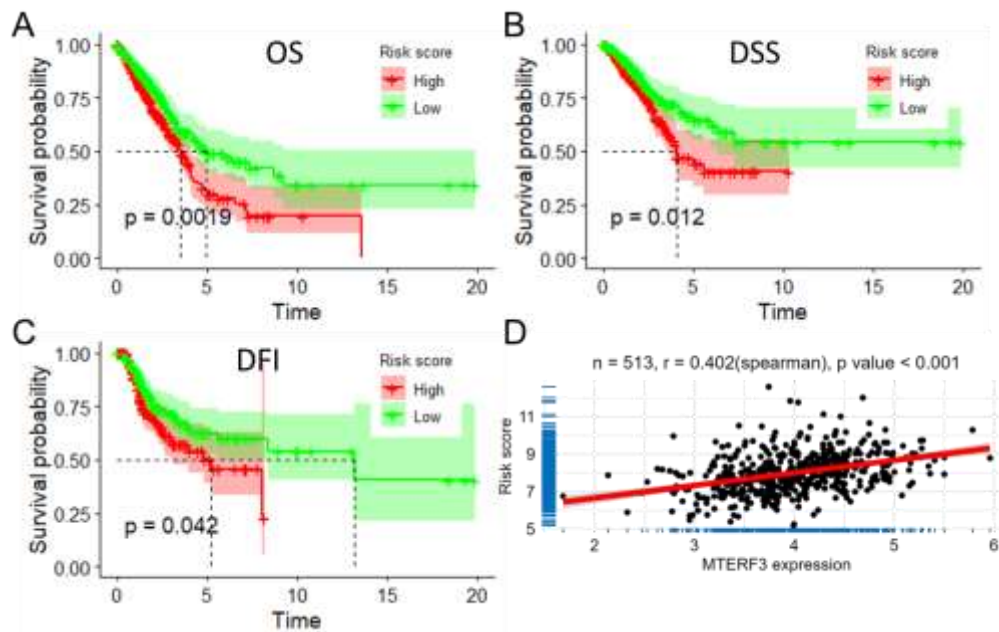
Figure S6. Nomogram predicting 1-year, 3-year and 5-year overall survival of lung adenocarcinoma patients. calibration plot for internal validation of the prognostic nomogram using TCGA-LUAD (A), GSE13213 (B) and GSE31210 (C) datasets. (D) The nomogram consists of the MRGs risk score and 8 clinical indicators based on the GSE31210 dataset. TCGA: The Cancer Genome Atlas; LUAD: lung adenocarcinoma; MRGs: mitophagy-related genes.
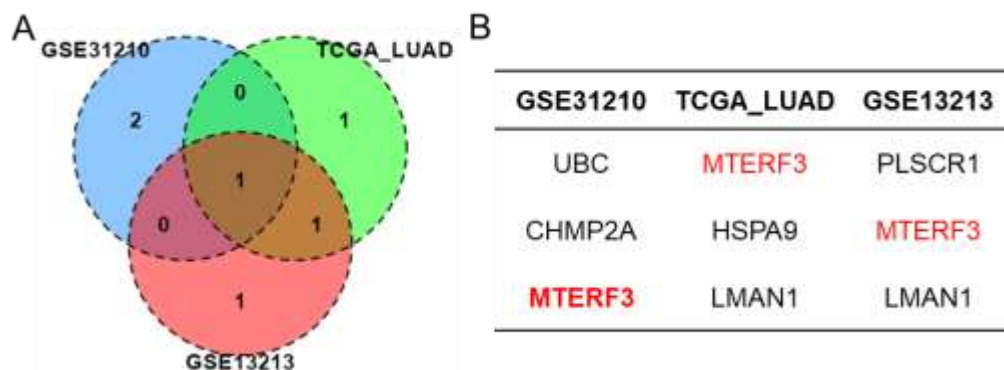
Figure S7. Volcano plots show the correlation between risk score and the expression of genes in the p38-MAPK pathway in TCGA-LUAD (A), GSE13213 (B) and GSE31210 (C) datasets. TCGA: The Cancer Genome Atlas; LUAD: lung adenocarcinoma.

Figure S8. Mitophagy risk score is associated with tumor suppress genes expression and tumor mutation burden. Volcano plots show the correlation between risk score and the expression of tumor suppress genes in TCGA-LUAD (A), GSE13213 (B) and GSE31210 (C) datasets. (D) Heatmap shows the correlation between risk score and the expression of tumor suppress genes in 3 datasets. (E) scatter plot shows the correlation between risk score and tumor mutation burden. TCGA: The Cancer Genome Atlas; LUAD: lung adenocarcinoma.
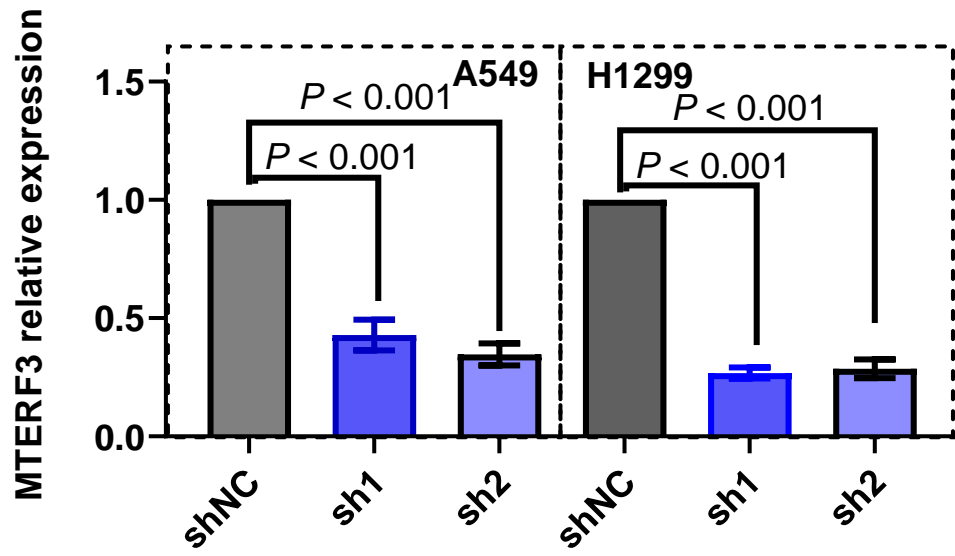
Figure S9. MTERF3 related to lung cancer prognosis. Kaplan–Meier curve of MTERF3 for OS (A), DSS (B), and DFI (C) in TCGA-LUAD dataset. (D) Scatter plot shows the correlation between risk score and MTERF3 expression. DSS, disease specific survival. DFI, disease free interval. OS, overall survival. LUAD, lung adenocarcinoma.

Figure S10. Identification of key MRG in the model. (A) The Venn diagram shows the intersection of the top three MRGs most correlated with risk scores in three datasets. (B) The table displays the top three MRGs most relevant to risk scores in each dataset. TCGA: The Cancer Genome Atlas; LUAD: lung adenocarcinoma; MRGs: mitophagy-related genes.

Figure S11. Validation of MTERF3 expression in LUAD cells transfected with MTERF3 knocked down plasmids.