Table S1 Pyroptosis-related genes derived from the GeneCards database

Gene symbol	Description	Category	Gifts	GC Id	Relevance score	GeneCards Link
GSDMD	Gasdermin D	Protein coding	39	GC08P143553	20.79	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSDMD
GSDME	Gasdermin E	Protein coding	31	GC07M024699	14.54	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSDME
NLRP3	NLR family pyrin domain containing 3	Protein coding	47	GC01P247415	12.89	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRP3
CASP4	Caspase 4	Protein coding	46	GC11M104942	9.79	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP4
GSDMB	Gasdermin B	Protein coding	36	GC17M039904	9.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSDMB
NLRC4	NLR family CARD domain containing 4	Protein coding	44	GC02M032224	8.04	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRC4
GSDMA	Gasdermin A	Protein coding	36	GC17P039962	7.49	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSDMA
GSDMC	Gasdermin C	Protein coding	32	GC08M129705	7.49	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GSDMC
CASP1	Caspase 1	Protein coding	50	GC11M105025	7.26	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP1
IL1B	Interleukin 1 beta	Protein coding	48	GC02M112829	7.21	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1B
NLRP1	NLR family pyrin domain containing 1	Protein coding	44	GC17M005499	7.02	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRP1
NAIP	NLR family apoptosis inhibitory protein	Protein coding	40	GC05M070968	6.17	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NAIP
PYCARD	PYD and CARD domain containing	Protein coding	43	GC16M031201	5.64	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PYCARD
DHX9	DExH-box helicase 9	Protein coding	40	GC01P182839	5.48	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DHX9
NLRP9	NLR family pyrin domain containing 9	Protein coding	34	GC19M055711	5.48	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRP9
APIP	APAF1 interacting protein	Protein coding	39	GC11M034854	5.19	https://www.genecards.org/cgi-bin/carddisp.pl?gene=APIP
AIM2	Absent In melanoma 2	Protein coding	41	GC01M159062	4.75	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AIM2
CASP3	Caspase 3	Protein coding	50	GC04M184627	3.93	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP3
DDX3X	DEAD-box helicase 3 X-linked	Protein coding	47	GC0XP041333	3.43	https://www.genecards.org/cgi-bin/carddisp.pl?gene=DDX3X
KCNQ1OT1	KCNQ1 opposite strand/antisense transcript 1	Rna gene	25	GC11M002661	3.36	https://www.genecards.org/cgi-bin/carddisp.pl?gene=KCNQ1OT1
FOXO3	Forkhead box O3	Protein coding	44	GC06P108559	3.26	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FOXO3
CPTP	Ceramide-1-phosphate transfer protein	Protein coding	31	GC01P001475	3.09	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CPTP
IL18	Interleukin 18	Protein coding	44	GC11M112143	2.83	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL18
HMGB1	High mobility group box 1	Protein coding	44	GC13M030456	2.51	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HMGB1
CASP5	Caspase 5	Protein coding	44	GC11M104995	2.45	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CASP5
GJA1	Gap junction protein alpha 1	Protein coding	50	GC06P121436	2.41	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GJA1
MIR30C1	MicroRNA 30c-1	Rna gene	21	GC01P040757	2.37	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR30C1
MIR214	MicroRNA 214	Rna gene	20	GC01M172234	2.35	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR214
MALAT1	Metastasis associated lung adenocarcinoma transcript 1	Rna gene	24	GC11P065806	2.33	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MALAT1
MIR22	MicroRNA 22	Rna gene	20	GC17M001713	2.33	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR22
TP53	Tumor protein P53	Protein coding	54	GC17M007661	2.28	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TP53
TET2	Tet methylcytosine dioxygenase 2	Protein coding	44	GC04P105145	2.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TET2
MIR125A	MicroRNA 125a	Rna gene	21	GC19P051720	2.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR125A
MIR155	MicroRNA 155	Rna gene	18	GC21P025573	2.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR155
EEF2K	Eukaryotic elongation factor 2 kinase	Protein coding	47	GC16P022217	2.18	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EEF2K
P2RX7	Purinergic receptor P2X 7	Protein coding	45	GC12P122829	2.18	https://www.genecards.org/cgi-bin/carddisp.pl?gene=P2RX7
FGF21	Fibroblast growth factor 21	Protein coding	40	GC19P048766	2.18	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FGF21
MIR135B	MicroRNA 135b	Rna gene	19	GC01M205448	2.13	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR135B
MALT1	MALT1 paracaspase	Protein coding	47	GC18P058671	2.11	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MALT1
STK4	Serine/threonine kinase 4	Protein coding	48	GC20P044966	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STK4
MST1	Macrophage stimulating 1	Protein coding	44	GC03M049683	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MST1
TREM2	Triggering receptor expressed on myeloid cells 2	Protein coding	43	GC06M042280	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TREM2
GZMA	Granzyme A	Protein coding	42	GC05P055102	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GZMA
GBP1	Guanylate binding protein 1	Protein coding	41	GC01M089052	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GBP1
ELAVL1	ELAV like RNA binding protein 1	Protein coding	41	GC19M007958	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ELAVL1
MIR9-1	MicroRNA 9-1	Rna gene	20	GC01M156420	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR9-1
MIR9-3	MicroRNA 9-3	Rna gene	19	GC15P089363	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR9-3
MIR9-2	MicroRNA 9-2	Rna gene	18	GC05M088666	2.06	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR9-2
HDAC6	Histone deacetylase 6	Protein coding	51	GC0XP048801	1.99	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HDAC6
SQSTM1	Sequestosome 1	Protein coding	48	GC05P179806	1.99	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SQSTM1
IRF3	Interferon regulatory factor 3	Protein coding	47	GC19M049659	1.99	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IRF3
STING1	Stimulator of interferon response CGAMP interactor 1	Protein coding	34	GC05M139476	1.99	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STING1
HNP1	Hypertensive nephropathy	Genetic locus	2	GC09U900671	1.99	https://www.genecards.org/cgi-bin/carddisp.pl?gene=HNP1
CAMP	Cathelicidin antimicrobial peptide	Protein coding	41	GC03P048266	1.66	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CAMP
PARP1	Poly(ADP-ribose) polymerase 1	Protein coding	49	GC01M226360	1.6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PARP1
GBP5	Guanylate binding protein 5	Protein coding	37	GC01M089259	1.6	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GBP5
NR1H2	Nuclear receptor subfamily 1 group H member 2	Protein coding	48	GC19P050329	1.53	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NR1H2
CTSG	Cathepsin G	Protein coding	44	GC14M024573	1.46	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CTSG
MKI67	Marker of proliferation Ki-67	Protein coding	44	GC10M128096	1.46	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MKI67
IL36G	Interleukin 36 gamma	Protein coding	38	GC02P112973	1.36	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL36G
IL36B	Interleukin 36 beta	Protein coding	35	GC02M113022	1.36	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL36B
ANO6	Anoctamin 6	Protein coding	39	GC12P045215	1.07	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANO6
FADD	Fas associated via death domain	Protein coding	47	GC11P070203	1.01	https://www.genecards.org/cgi-bin/carddisp.pl?gene=FADD
NLRP7	NLR family pyrin domain containing 7	Protein coding	43	GC19M054923	1.01	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRP7
TNF	Tumor necrosis factor	Protein coding	51	GC06P047305	0.94	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TNF
VIM	Vimentin	Protein coding	50	GC10P017227	0.94	https://www.genecards.org/cgi-bin/carddisp.pl?gene=VIM
CAPN1	Calpain 1	Protein coding	49	GC11P065198	0.94	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CAPN1
PRTN3	Proteinase 3	Protein coding	44	GC19P000840	0.87	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRTN3
MEFV	MEFV innate immunity regulator, pyrin	Protein coding	43	GC16M003281	0.87	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MEFV
SERPINB1	Serpin family B member 1	Protein coding	40	GC06M002833	0.87	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SERPINB1
ALK	ALK receptor tyrosine kinase	Protein coding	51	GC02M029156	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ALK
SIRT1	Sirtuin 1	Protein coding	49	GC10P067884	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=SIRT1
BIRC3	Baculoviral IAP repeat containing 3	Protein coding	46	GC11P102317	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BIRC3
BIRC2	Baculoviral IAP repeat containing 2	Protein coding	45	GC11P102347	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BIRC2
UBE2D2	Ubiquitin conjugating enzyme E2 D2	Protein coding	44	GC05P139526	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=UBE2D2
APOL1	Apolipoprotein L1	Protein coding	42	GC22P036253	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=APOL1
LY96	Lymphocyte antigen 96	Protein coding	42	GC08P073991	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LY96
GLMN	Glomulin, FKBP associated protein	Protein coding	40	GC01M092246	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GLMN
IRGM	Immunity related GTPase M	Protein coding	38	GC05P150846	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IRGM
NLRP13	NLR family pyrin domain containing 13	Protein coding	35	GC19M055892	0.77	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NLRP13
TUBB6	Tubulin beta 6 class V	Protein coding	41	GC18P012307	0.68	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TUBB6
PYDC2	Pyrin domain containing 2	Protein coding	24	GC03P191461	0.53	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PYDC2
AKT1	AKT serine/threonine kinase 1	Protein coding	54	GC14M104769	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=AKT1
EGFR	Epidermal growth factor receptor	Protein coding	54	GC07P055019	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=EGFR
TP63	Tumor protein P63	Protein coding	48	GC03P189598	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TP63
ATF6	Activating transcription factor 6	Protein coding	47	GC01P161766	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ATF6
IFI16	Interferon gamma inducible protein 16	Protein coding	42	GC01P158969	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IFI16
POP1	POP1 homolog, ribonuclease P/MRP subunit	Protein coding	40	GC08P098117	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=POP1
ORMDL3	ORMDL sphingolipid biosynthesis regulator 3	Protein coding	39	GC17M039921	0.34	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ORMDL3
BTK	Bruton tyrosine kinase	Protein coding	53	GC0XM101349	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BTK
STAT3	Signal transducer and activator of transcription 3	Protein coding	52	GC17M042313	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=STAT3
NFKB1	Nuclear factor kappa B subunit 1	Protein coding	52	GC04P102501	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=NFKB1
BCL2	BCL2 apoptosis regulator	Protein coding	51	GC18M063123	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BCL2
TLR2	Toll like receptor 2	Protein coding	51	GC04P153684	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=TLR2
ANXA2	Annexin A2	Protein coding	48	GC15M060347	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANXA2
BECN1	Beclin 1	Protein coding	46	GC17M042810	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BECN1
CD14	CD14 molecule	Protein coding	44	GC05M140631	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD14
IL13	Interleukin 13	Protein coding	44	GC05P132656	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL13
CHI3L1	Chitinase 3 like 1	Protein coding	43	GC01M203148	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CHI3L1
PANX1	Pannexin 1	Protein coding	43	GC11P094128	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=PANX1
LRPPRC	Leucine rich pentatricopeptide repeat containing	Protein coding	42	GC02M043850	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LRPPRC
CXCL8	C-X-C motif chemokine ligand 8	Protein coding	41	GC04P073740	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCL8
IL13RA2	Interleukin 13 receptor subunit alpha 2	Protein coding	41	GC0XM115003	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL13RA2
IL32	Interleukin 32	Protein coding	40	GC16P004242	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL32
BST2	Bone marrow stromal cell antigen 2	Protein coding	39	GC19M017403	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=BST2
LYST	Lysosomal trafficking regulator	Protein coding	38	GC01M235661	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=LYST
GPER1	G protein-coupled estrogen receptor 1	Protein coding	37	GC07P001188	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=GPER1
CLEC5A	C-type lectin domain containing 5A	Protein coding	34	GC07M141927	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=CLEC5A
MIR223	MicroRNA 223	RNA gene	21	GC0XP066018	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR223
MIR20B	MicroRNA 20b	RNA gene	15	GC0XM134217	0.24	https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR20B

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Table S2 Results of 26 pyroptosis-related genes identified in differentially expressed analysis in the TCGA-LUAD dataset

Genes	Base mean	LogFC	LfcSE	Stat.	P value	FDR
MKI67	3533.056	−3.32718	0.166517	−19.981	8.06E−89	7.90E−87
NLRC4	254.7377	2.017568	0.104854	19.24172	1.66E−82	8.11E−81
PARP1	9166.919	−1.1725	0.08541	−13.7278	6.92E−43	2.26E−41
IL36G	28.50111	−4.0338	0.31024	−13.0022	1.19E−38	2.91E−37
AIM2	432.8062	−2.83864	0.222915	−12.7342	3.82E−37	7.49E−36
GSDMB	1282.436	−1.89962	0.152084	−12.4906	8.40E−36	1.37E−34
GSDMC	362.4923	−2.73436	0.226562	−12.0689	1.54E−33	2.16E−32
BTK	723.5322	1.323927	0.113146	11.70105	1.26E−31	1.54E−30
MEFV	79.08195	1.588184	0.142912	11.11304	1.08E−28	8.85E−28
POP1	433.3758	−1.04772	0.094749	−11.0579	2.01E−28	1.51E−27
CAMP	39.16229	2.497897	0.237022	10.53866	5.73E−26	3.74E−25
GPER1	216.5156	1.967691	0.190281	10.34097	4.60E−25	2.82E−24
VIM	38237.57	1.050962	0.10463	10.04461	9.70E−24	5.59E−23
TUBB6	2654.095	1.161233	0.12122	9.579564	9.75E−22	5.31E−21
MST1	315.0309	−1.59668	0.172427	−9.26003	2.04E−20	1.00E−19
CASP5	26.71728	1.267633	0.151058	8.39168	4.79E−17	2.13E−16
IL13	4.925103	1.496938	0.187722	7.974239	1.53E−15	6.26E−15
CTSG	80.79507	1.722087	0.231224	7.447685	9.50E−14	3.21E−13
KCNQ1OT1	417.8221	−1.23114	0.172603	−7.13275	9.84E−13	3.11E−12
NLRP7	17.22144	−1.27272	0.187501	−6.78777	1.14E−11	3.28E−11
GJA1	5957.535	1.058294	0.161846	6.5389	6.20E−11	1.74E−10
CHI3L1	8116.59	−1.41656	0.225666	−6.27724	3.45E−10	9.13E−10
GSDMA	67.40323	−1.17423	0.192915	−6.08679	1.15E−09	2.82E−09
MIR135B	2.299623	−1.24253	0.233194	−5.32833	9.91E−08	2.26E−07
FGF21	2.252621	−1.65782	0.37071	−4.47201	7.75E−06	1.62E−05
NLRP13	2.261375	−1.4579	0.390676	−3.73173	0.00019	0.000333

TCGA-LUAD, The Cancer Genome Atlas-lung adenocarcinoma; FC, fold change; lfcSE, standard error for log2 fold change; FDR, false discovery rate.

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Table S3 Results of 4 key genes in multivariate Cox regression analysis in the TCGA-LUAD dataset

Genes	Coefficient	HR	z	P value
MKI67	0.13	1.1 (1.0–1.3)	2.3	0.024
BTK	–0.27	0.77 (0.67–0.88)	–3.9	1.00E–04
TUBB6	0.23	1.3 (1.1–1.5)	3	0.0032
MST1	–0.14	0.87 (0.76–1.00)	–1.9	0.055

TCGA-LUAD, The Cancer Genome Atlas-lung adenocarcinoma; HR, hazard ratio.

Table S4 Results of clinical variables and 4-gene signature riskScore in univariate Cox regression analysis in the TCGA-LUAD dataset

Variables	Coefficient	HR (95% CI for HR)	Wald test	z	P value
Gender	0.057	1.1 (0.76–1.5)	0.11	0.33	0.74
pathologic_N_stage	–0.92	0.4 (0.28–0.56)	28	–5.3	1.20E–07
pathologic_M_stage	0.61	1.8 (1–3.3)	4.4	2.1	0.037
pathologic_T_stage	0.46	1.6 (1.3-1.9)	21	4.5	5.90E–06
tumor_stage	0.46	1.6 (1.3–1.8)	32	5.7	1.30E–08
Age	–0.34	0.71 (0.4–1.3)	1.4	–1.2	0.24
riskScore	0.67	2 (1.6–2.4)	49	7	2.30E–12

TCGA-LUAD, The Cancer Genome Atlas-lung adenocarcinoma; HR, hazard ratio; CI, confidence interval.

Table S5 Results of clinical variables and 4-gene signature riskScore in multivariate Cox regression analysis in the TCGA-LUAD dataset

Variables	Coefficient	HR	z	P value
pathologic_N_stage	–0.56	0.57 (0.34–0.97)	–2.1	0.036
pathologic_M_stage	0.065	1.1 (0.42–2.7)	0.14	0.89
pathologic_T_stage	0.25	1.3 (1.0–1.6)	2.2	0.03
tumor_stage	0.15	1.2 (0.81–1.7)	0.82	0.41
riskScore	0.6	1.8 (1.5–2.2)	5.8	5.20E–09

TCGA-LUAD, The Cancer Genome Atlas-lung adenocarcinoma; HR, hazard ratio.

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