

1 **Supplementary Table S1**

Antibody	Supplier	Catalog No.
STK19	Abclonal	A7574
PI3K p110δ	Abclonal	A19742
phospho-Akt (Ser473)	CST	#4060
pan-Akt	CST	#4691
p-RIPK3 (Ser227)	CST	#93654
cleaved Caspase-8 (Asp374)	CST	#9496
Caspase-8	CST	#4790
p-RIPK1 (Ser166)	CST	#44590
RIPK1	CST	#3493
NLRP3	CST	#15101
cleaved Caspase-3 (Asp175)	CST	#9664
cleaved PARP	CST	#5625
p-MLKL	Proteintech	82090-2-RR
MLKL	Proteintech	66675-1-Ig
NRAS	Proteintech	18296-1-AP
β-actin	Proteintech	66009-1-Ig

2

3 **Supplementary Table S2**

Name	Sequence 5' to 3'
STK19-F	AGCA GGAC CAAA TGAC ACAG ACC
STK19-R	GACG GTGA GGAC TCCA GCAT TC
PHLDA1-F	TCAG CCTC AGCC GCAA CC
PHLDA1-R	GAGT GTGG ATGT GGAT GTGG ATG
ETV4-F	ACAG ACGG ACTT CGCC TACG
ETV4-R	GGTT TCTC ATAG CCAT AGCC CATG
SPRY2-F	TGAT TGAC TATG GGAC TTGT GTAT GC
SPRY2-R	AGCA CAGT TGTC CTCA TCAT CATT AG
DUSP4-F	CCTG ATGA TGAA GAAA CGGG TGAG
DUSP4-R	GCTG AAGT TGGG CGAG ATGA TG
IL1B-F	GCAC CTGT ACGA TCAC TGAA CTG
IL1B-R	CCAC TTGT TGCT CCAT ATCC TGTC
TNF-F	GCTC CAGG CGGT GCTT GTTC
TNF-R	CATG GGCT ACAG GCTT GTCA CTC
IL6-F	GGTG TTGC CTGC TGCC TTCC
IL6-R	GTTC TGAA GAGG TGAG TGGC TGTC
PYCARD-F	GGTC ACAA ACGT TGAG TGGC
PYCARD-R	AGAG CTTC CGCA TCTT GCTT
ZBP1-F	AGAA TCCT GCAG GTGC TGAC
ZBP1-R	GGAC TTGG TTGA GCTC CCTC
NLRP12-F	AGCT GCTC ATCA CCCA CTTC

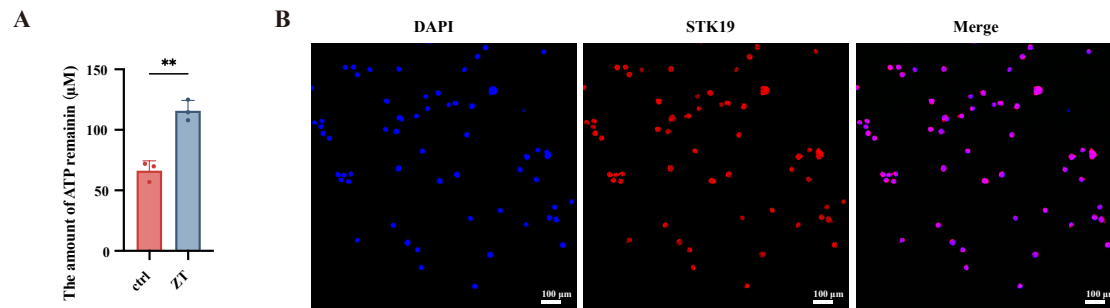
NLRP12-R

GGTA TCCC TCAC CAGG TCCT

Supplementary Table S3

Name	TRCN IDs	Sequence 5' to 3'
shSTK19#1	TRCN0000195656	CCATGGAAAGTGGAACCAGAA
shSTK19#2	TRCN0000199316	CCAGGATGAGTGTCTGGGCTCT
shSTK19#3	TRCN0000226394	ATGGAAAGTGGAACCAGAAT
shSTK19#4	TRCN0000199490	GCTGTGGCTGTTCCCTTTCGT

Supplementary Figure S1

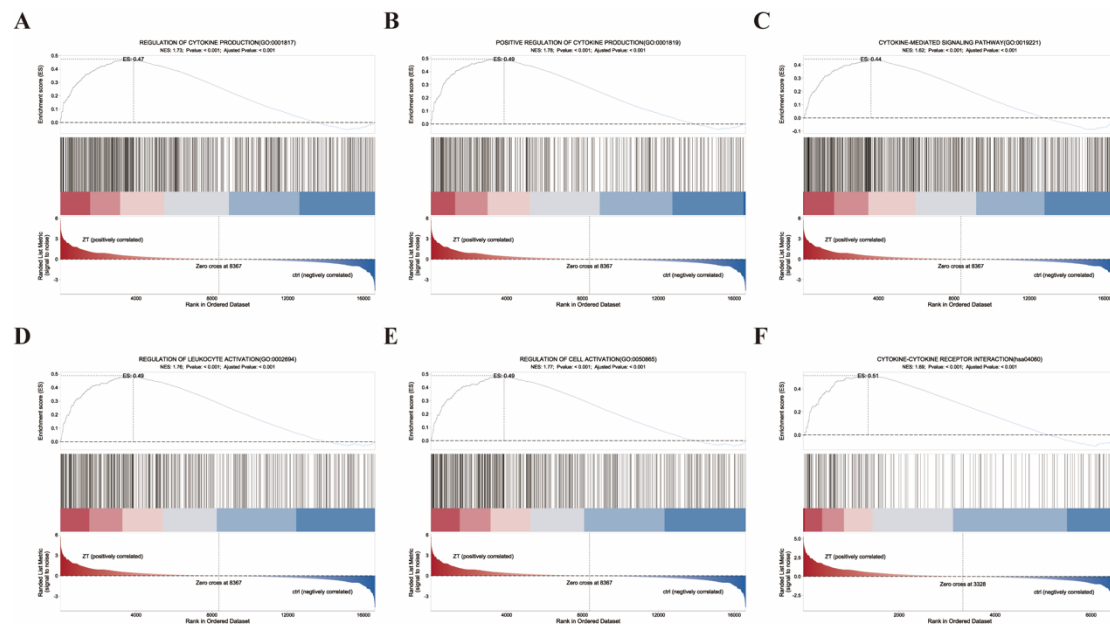


Supplementary Figure S1. STK19 subcellular localization and in vitro kinase assay supporting STK19-associated kinase activity

(A) *In vitro* kinase assay performed using recombinant STK19 and NRAS proteins in the presence or absence of ZT. Residual ATP levels were measured using a kinase activity assay. Increased residual ATP in the ZT-treated group is consistent with reduced STK19-associated kinase activity.

(B) Immunofluorescence staining showing the subcellular localization of STK19 in AML cells, with signal detected in both the nucleus and cytoplasm. Representative images are shown.

Supplementary Figure S2

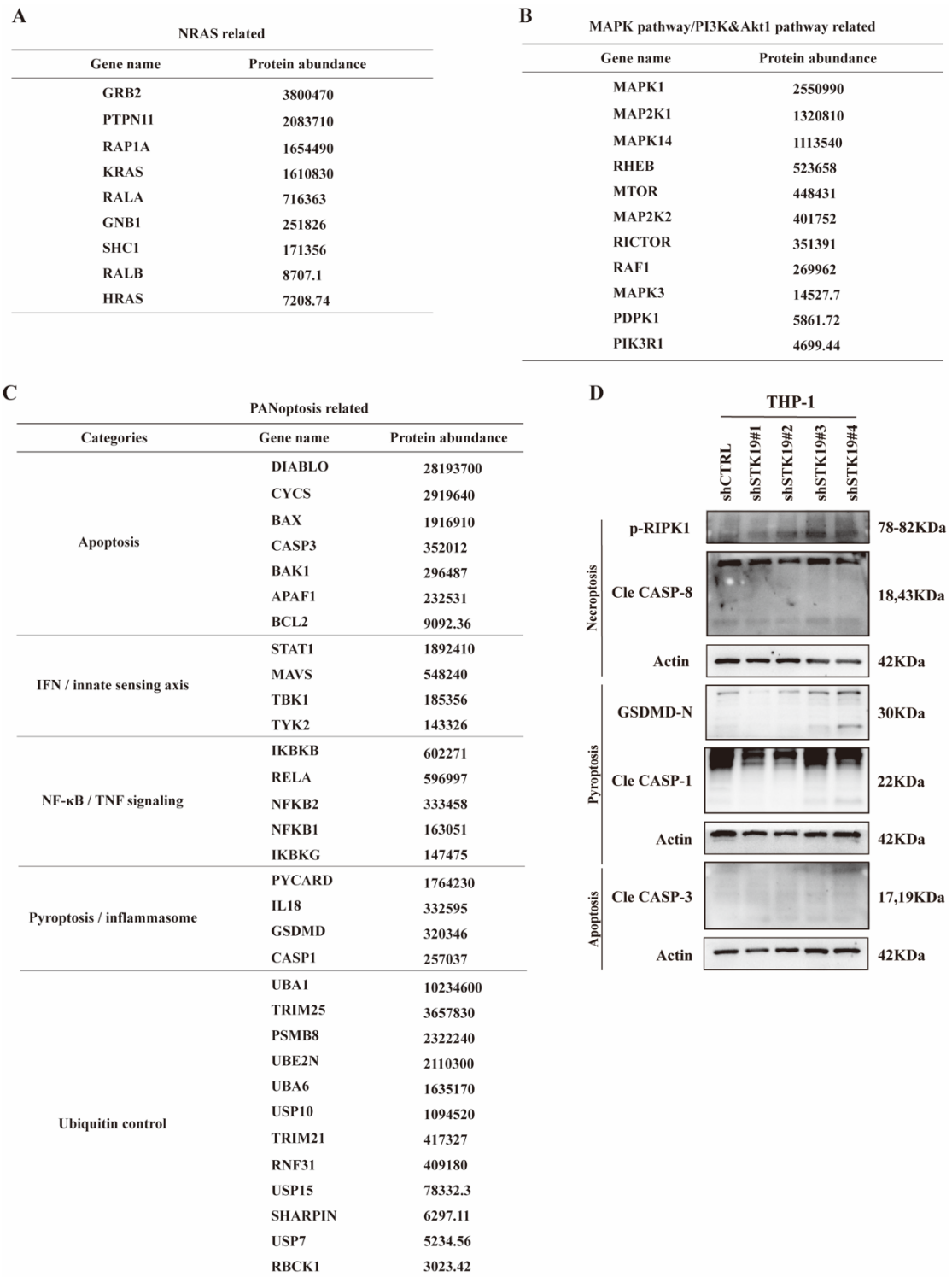


Supplementary Figure S2. Additional GSEA plots showing enrichment of inflammation- and cytokine-related pathways in THP-1 cells following ZT treatment

(A–F) Representative GSEA plots showing enrichment of additional inflammation- and cytokine-related gene sets in THP-1 cells treated with ZT versus vehicle, including regulation of cytokine production (A), positive regulation of cytokine production (B), cytokine-mediated signaling pathway (C), regulation of leukocyte activation (D), regulation of cell activation (E), and cytokine–cytokine receptor interaction (F).

Normalized enrichment scores (NES), nominal P values, and adjusted P values are indicated in each panel.

Supplementary Figure S3



Supplementary Figure S3. Proteomic changes associated with NRAS signaling, MAPK/PI3K–AKT pathways, and PANoptosis-related modules following ZT treatment

(A) Proteins associated with NRAS-related signaling identified in quantitative proteomic analysis of THP-1 cells treated with vehicle or ZT.

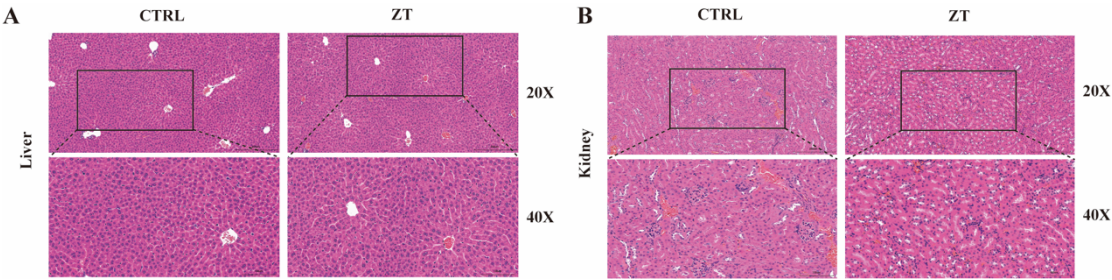
(B) Differentially expressed proteins associated with the MAPK and PI3K–AKT pathways.

(C) Differentially expressed proteins associated with PANoptosis-related or inflammatory cell

death-related modules.

(D) Immunoblot validation showing coordinated upregulation of key PANoptosis-associated proteins in STK19-depleted cells.

Supplementary Figure S4



Supplementary Figure S4. Histological evaluation of liver and kidney tissues in vehicle- and ZT-treated PDX mice

(A) Representative H&E staining images of liver sections from vehicle- and ZT-treated PDX mice.

(B) Representative H&E staining images of kidney sections from vehicle- and ZT-treated PDX mice.

These data provide histological assessment of major organ toxicity following ZT treatment *in vivo*.

Scale bars are indicated in the images.