

Supplementary material

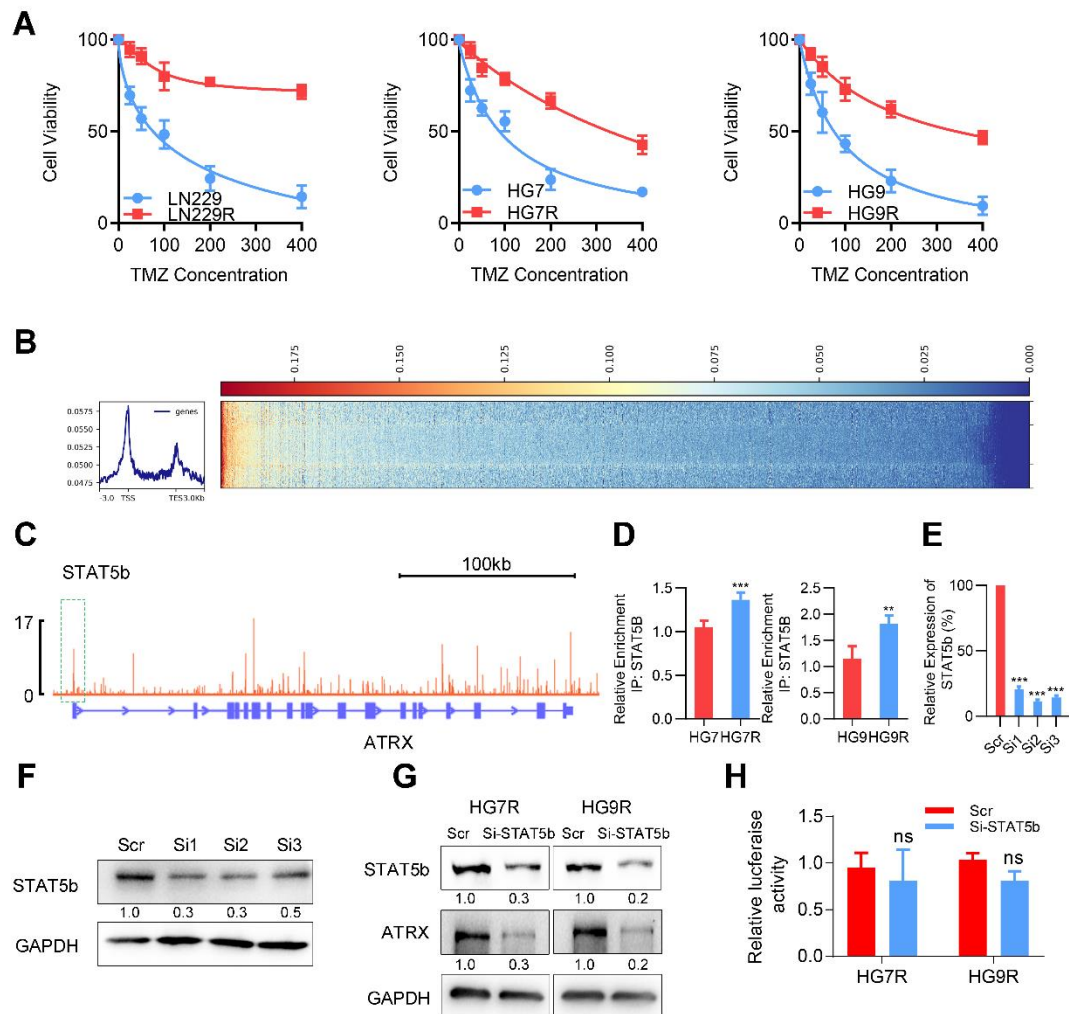


Figure S1. STAT5b is bound to the ATRX promoter region and is involved in ATRX expression.

(A) CCK-8 assays of TMZ-resistant and parental GBM cells upon TMZ treatment at the indicated concentrations for 72 hours (n=3). (B) Heatmap showing the read counts within a region spanning ± 3 kb around TSS in the whole genome. (C) IGV browser image showing STAT5b enrichment in ATRX promoter region. (D) ChIP-PCR analysis of ATRX promoter regions with STAT5b enrichment. (E-F) Validation of siRNAs targeting STAT5b performed by qRT-PCR and Western blot in HG7R cells. (G) Decreased ATRX protein expression STAT5b knockdown. (H) The transcription activity

of STAT5b in the promoter region of *ATRX* detected by luciferase reporter assay. Error bars indicated mean $\pm$ SD. “ns” means no significant, Student’s *t*-test.

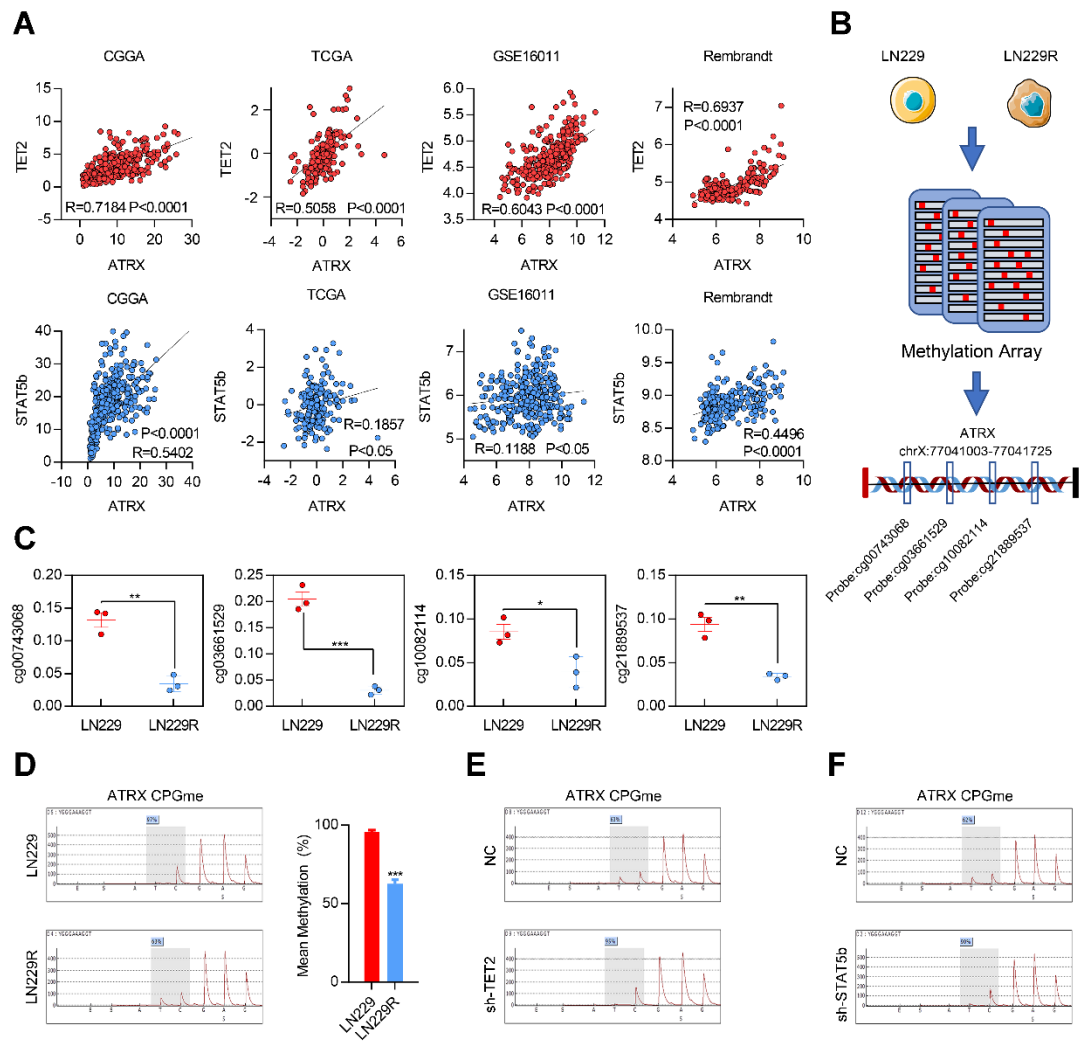


Figure S2. STAT5b/TET2 are response for ATRX hypomethylation

(A) Pearson correlation analysis between the *STAT5b/TET2* and *ATRX* levels in GBM samples (CGGA n=388, TCGA n=160, GSE16011 n=284, Rembrandt n=227). (B) Schematic of the DNA methylation microarray. Schematic used elements from Servier Medical Art: <https://smart.servier.com>. (C) DNA methylation microarray showing lower methylation in *ATRX* promoter region in LN229R cells compared with parental cells. Error bars indicate mean $\pm$ SD. * P < 0.05, ** P < 0.01, *** P < 0.001; Student's *t*-test. (D) Validation of *ATRX* methylation levels by pyrosequencing in LN229 and 229R cells. (E-F) Validation of *ATRX* methylation levels by

pyrosequencing in 229R after knocking down *TET2* or *STAT5b*. Error bars indicate mean $\pm$ SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; Student's *t*-test.

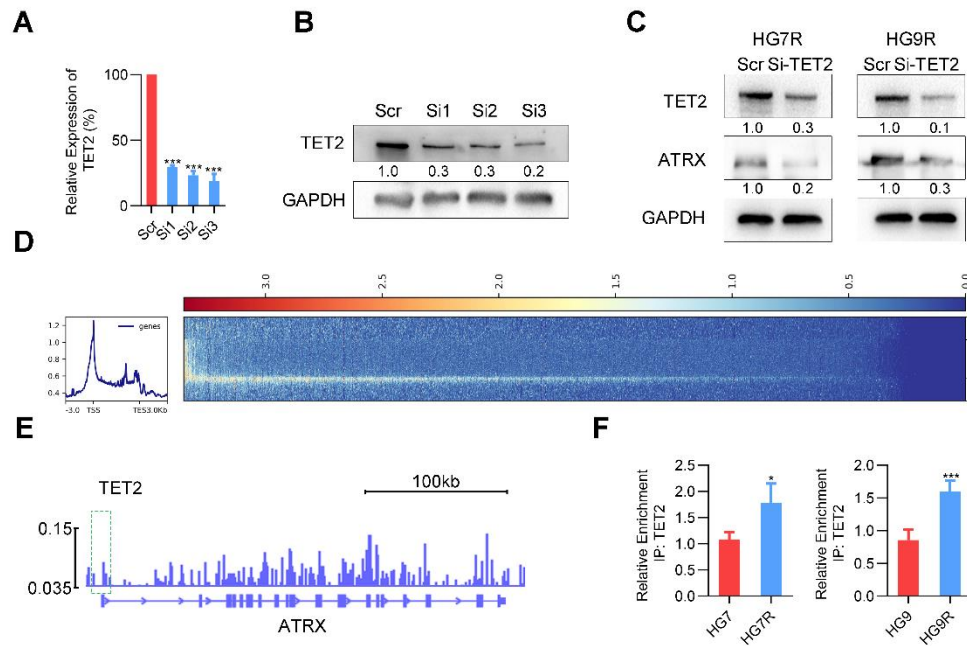


Figure S3. TET2 is enriched in *ATRX* promoter region and involved in *ATRX* expression.

(A-B) Validation of siRNAs targeting TET2 by qRT-PCR and western blotting in HG7R cells. (C) Decreased ATRX protein expression with TET2 knockdown in HG7R and HG9R cells. (D) Heatmap showed the read counts within a region spanning ± 3 kb around TSS in the whole genome. (E) The IGV browser image showing TET2 enrichment in *ATRX* promoter region. (F) ChIP-qPCR analysis of *ATRX* promoter regions with TET2 enrichment.

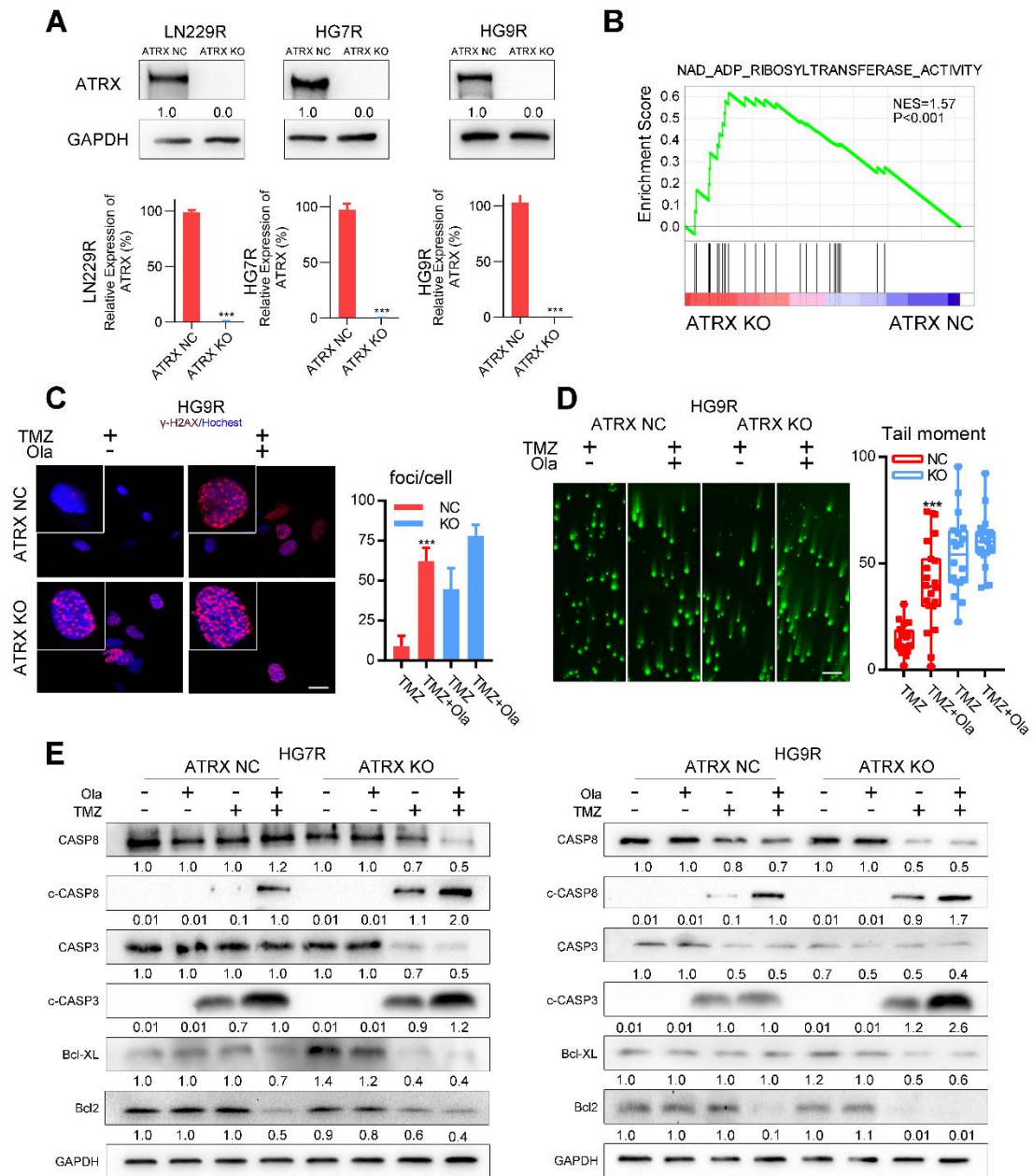


Figure S4. Activity and expression of apoptotic and DNA damage markers in *ATR* NC and *ATR* KO cells treated with TMZ and (or) olaparib.

(A) Validation of CRISPR-Cas9 mediated *ATR* knocking out performed by qRT-PCR and western blotting in LN229R, HG9R, HG7R cells. (B) GSEA of NAD ADP ribosyltransferase activity pathway was performed between *ATR* NC and *ATR* KO cells. (C) γ -H2AX is shown in

red and nucleus in blue. Bar plots showing the statistics of immunofluorescence assays in HG9R. Scales: 20 μm . (D) Comet assays measuring the DNA damage status in *ATR*X NC and *ATR*X KO cells treated with TMZ or combination of TMZ and olaparib in HG9R. Scales: 100 μm . Error bars indicate mean $\pm$ SD. *** $P < 0.001$, Student's *t*-test. (E) Levels of CASP 8, c-CASP 8, CASP3, c-CASP 3, BCL-XL and BCL 2 detected by western blotting in *ATR*X NC and *ATR*X KO cells treated with TMZ and (or) olaparib.

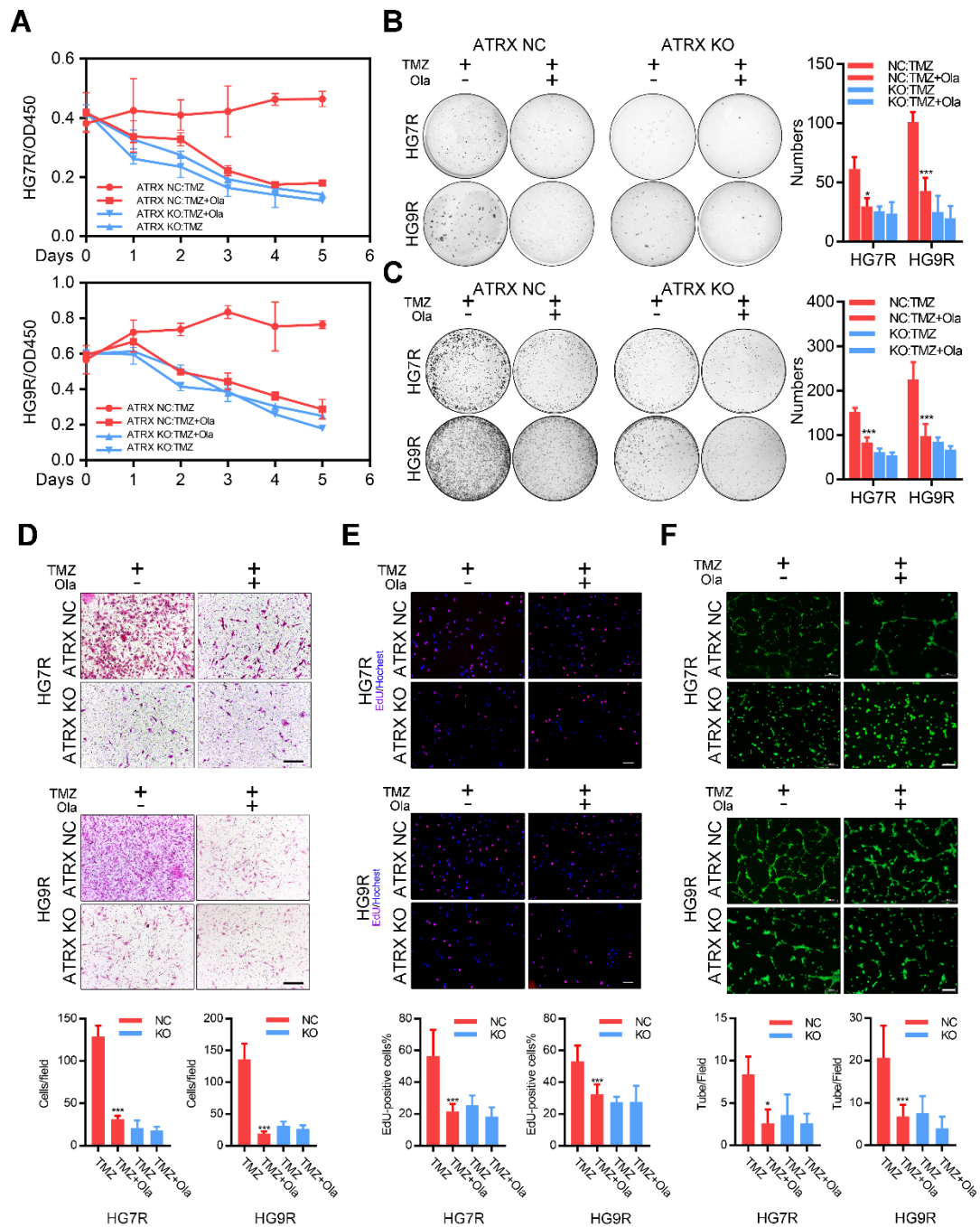


Figure S5. Proliferation, invasive ability and vascular mimicry of *ATRX* NC and *ATRX* KO cells treated with TMZ alone or a combination of TMZ and olaparib.

(A) CCK-8 assays showing the proliferation of *ATRX* NC and *ATRX* KO cells treated with TMZ or a combination of TMZ and olaparib. (B) Soft agar colony formation assay of *ATRX* NC and *ATRX* KO cells treated with TMZ or a combination of TMZ and olaparib. (C) Colony formation assay of *ATRX* NC and *ATRX* KO cells treated with TMZ or a combination of TMZ and olaparib. (D)

Transwell assays of *ATRX* NC and *ATRX* KO HG7R, HG9R cells treated with TMZ or combination of TMZ and olaparib. Scale: 200 μ m. (E) EdU assays (EdU in red and nucleus in blue) of *ATRX* NC and *ATRX* KO HG7R, HG9R cells treated with TMZ or a combination of TMZ and olaparib. Scale: 100 μ m. (F) Vascular mimicry assays of *ATRX* NC and *ATRX* KO HG7R, HG9R cells treated with TMZ or combination of TMZ and olaparib. Scale: 100 μ m. Error bars indicate mean $\pm$ SD. * $P < 0.05$, *** $P < 0.001$; Student's *t*-test.

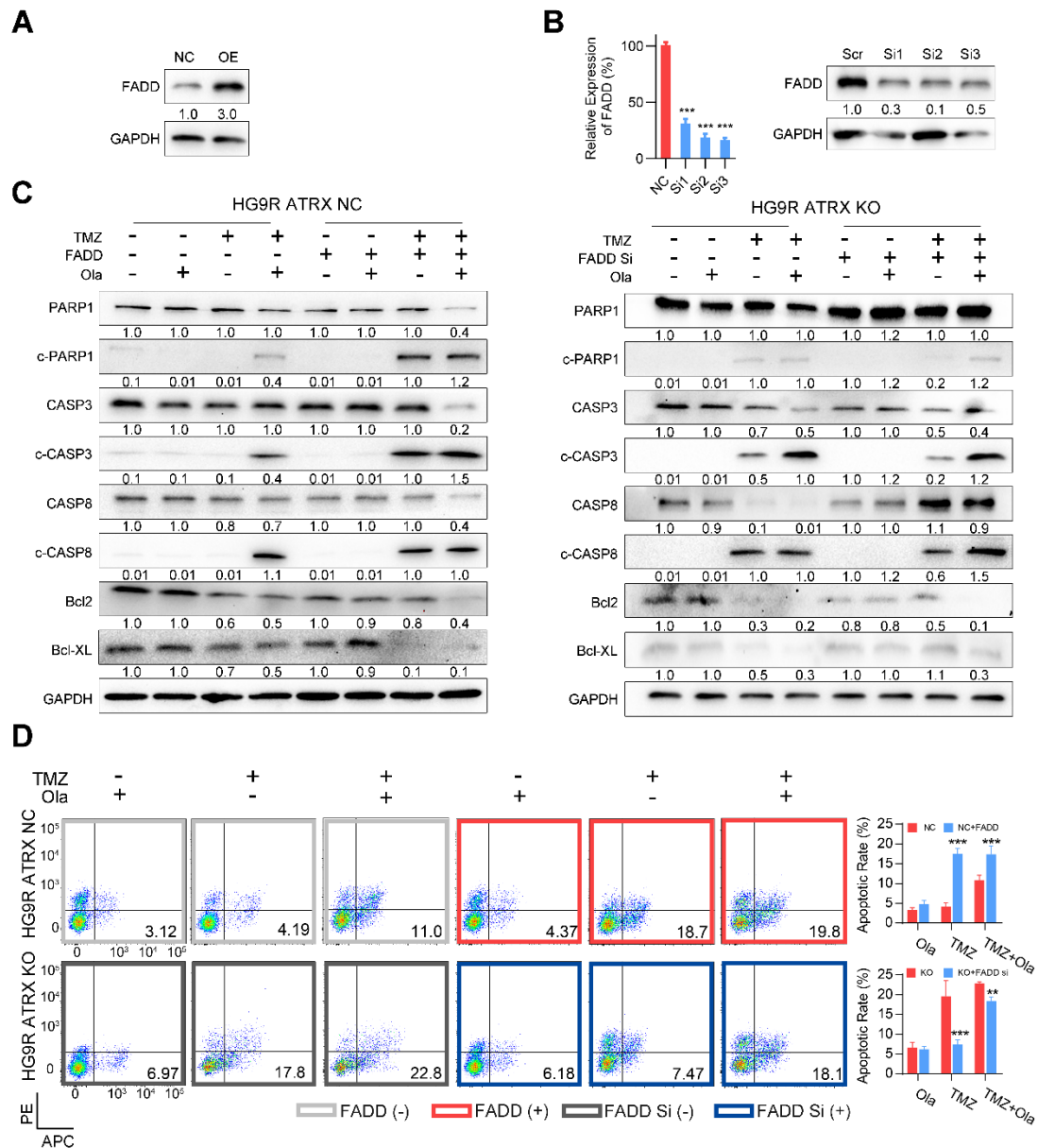


Figure S6. FADD inhibits the stabilization of PARP1 by ATRX and enhances TMZ induced apoptosis.

(A) Validation of FADD overexpression in HG7R cells by Western blotting. (B) Validation of FADD knockdown in HG7R cells. (C) Levels of PARP1, c-PARP1, CASP 8, c-CASP 8, CASP3, c-CASP 3, BCL-XL and BCL 2 detected by Western blotting in *ATR*X NC and *ATR*X KO cells with *FADD* overexpression or knockdown treated with TMZ and (or) olaparib. (D) Cell apoptosis analysis showing the apoptosis of HG9R NC and HG9R KO cells with FADD overexpression or knockdown treated with TMZ and (or) olaparib. ** $P < 0.01$, *** $P < 0.001$, Student's *t*-test.

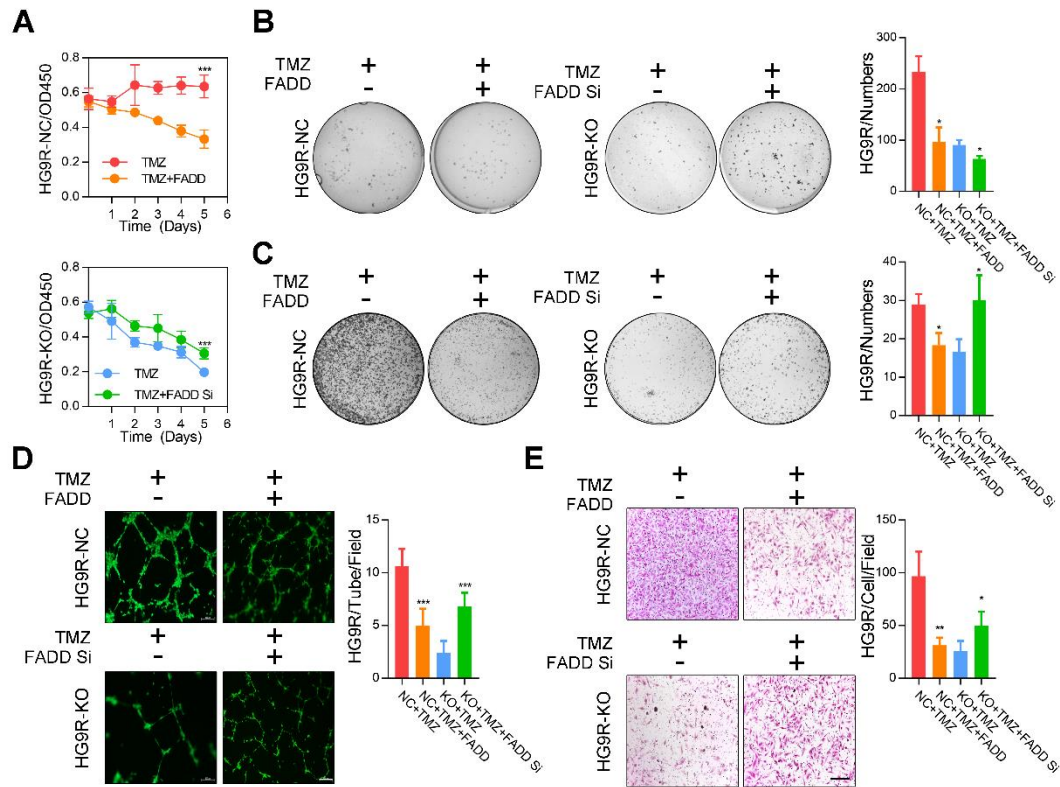


Figure S7. Proliferation, invasive ability and vascular mimicry of *ATRX* NC and *ATRX* KO HG9R cells with *FADD* overexpression or knockdown treated with TMZ.

(A) CCK-8 assays in *ATRX* NC and *ATRX* KO HG9R cells with FADD overexpression or knockdown treated with TMZ. (B-C) Soft agar colony and colony formation assays in *ATRX* NC and *ATRX* KO HG9R cells with FADD overexpression or knockdown treated with TMZ. (D) Vascular mimicry assays of *ATRX* NC and *ATRX* KO HG9R cells treated FADD overexpression or knockdown treated with TMZ. (E) Transwell assays of *ATRX* NC and *ATRX* KO HG9R cells with FADD overexpression or knockdown treated with TMZ. Scale: 200 μ m. The statistics was showed in bar plots. Error bars indicated mean $\pm$ SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; Student's *t*-test.

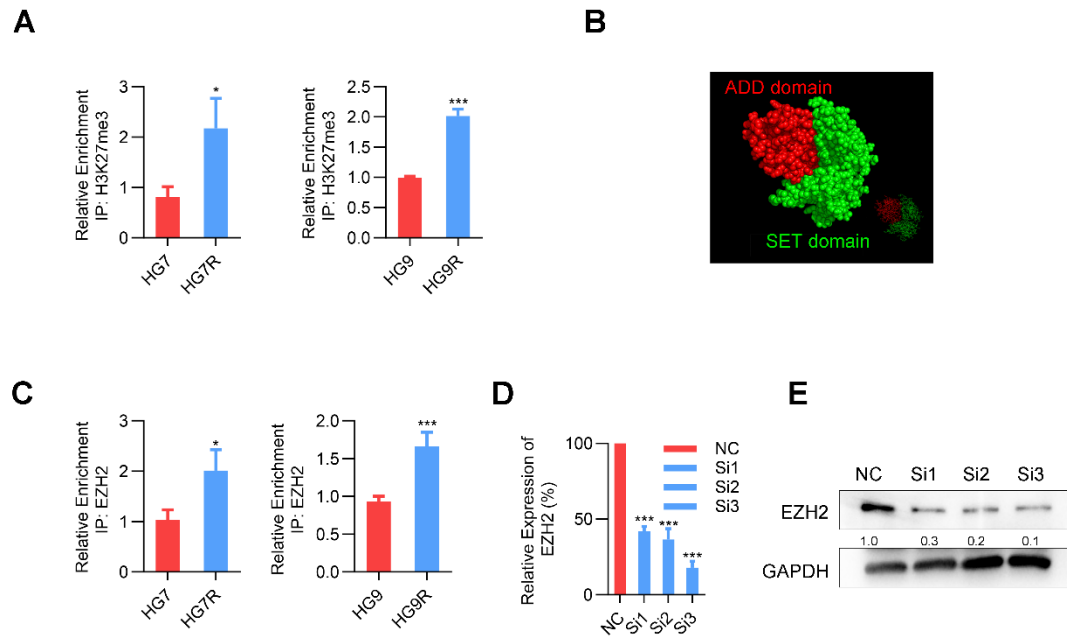


Figure S8. Enrichment of H3K27me3 and EZH2 in *FADD* promoter region, and prediction of ATRX binding to EZH2.

(A) ChIP-PCR analyses of *FADD* promoter regions with antibodies targeting H3K27me3 in HG7R and HG9R cells and their parental cells. (B) Model of the binding regions of ATRX and EZH2. Cartoon representation of the ATRX- EZH2 crystal structure. ATRX is colored red. EZH2 is colored gray. (C) ChIP-PCR analyses of *FADD* promoter regions with antibodies targeting EZH2 in HG7R and HG9R cells and their parental cells. (D-E) Validation of EZH2 knockdown in HG7R cells by qRT-PCR and western blotting.

Supplementary Table 1. The sequence of the sgRNAs and siRNAs.

CRISPR	Name	Sequence (5'-3')	
CRISPR	ATRX-KO-sgRNA-1	TCGTGACGATCCTGAAGACT	
CRISPR	ATRX-KO-sgRNA-2	ACTATGCAGAGCTTGCCAAA	
CRISPR	ATRX-KO-sgRNA-3	ACATACTTTGTTACAATTGA	
Assay	Name	Sequence sense (5'-3')	Sequence anti-sense (5'-3')
Gene Silencing	si-STAT5b-1/sh-STAT5b-1	GCAGAGUUACAGUCACAAAGU	UUUGUGACUGUAAACUCUGCAU
Gene Silencing	si-STAT5b-2/sh-STAT5b-2	GCGAGUCUGCUACUGCUAAAG	UUAGCAGUAGCAGACUCGCAG
Gene Silencing	si-STAT5b-3/sh-STAT5b-3	CGAGUCUGCUACUGCUAAAGC	UUUAGCAGUAGCAGACUCGCA
Gene Silencing	si-TET2-1/sh-TET2-1	CGAUUUGAGUGAUAGAAGAAG	UUUCUUAUCACUAAAUCGGA
Gene Silencing	si-TET2-2/sh-TET2-2	GGUGCUUACUUAAGCAAAGC	UUUGCUUGAAGUAAGCACCAU
Gene Silencing	si-TET2-3/sh-TET2-3	GGAGCAGAAGUCACAACAAGC	UUGUUGUGACUUCUGCUCCUG
Gene Silencing	si-FADD-1	GCGAGUCUCUUAUUCUAA	UUAGGAAUAAGAGGACUGC
Gene Silencing	si-FADD-2	GCGAGCUGACCGAGCUAAGU	UUGAGCUCGGUCAGCUCGCUG
Gene Silencing	si-FADD-3	CGAUGUCAUGGAACUCAGACG	UCUGAGUCCAUGACAUCGGG
Gene Silencing	si-EZH2-1	GGAUUGGUACUUUCAUUGAAGA	UUCAAUGAAAGUACCAUCCUG
Gene Silencing	si-EZH2-2	CCUCAAUUGUUCCAGAUAAAG	UUUUCUGGAAACAUUGAGGAA
Gene Silencing	si-EZH2-3	GCAAAGUACUGUAAGAAUAAU	UAUUCUUAACAGUACUUUGCAA

Supplementary Table 2. The details of primary antibodies used for western blot, ChIP, immunoprecipitation, immunohistochemistry and immunofluorescence.

Gene	Manufactory	Catalog number	Application
ATR	Cell Signaling Technology	#14820	Western blot/ChIP/Immunoprecipitation
ATR	Boster	A00203-1	Immunohistochemistry/Immunofluorescence
γ -H2AX	Cell Signaling Technology	#9718	Western blot/Immunohistochemistry
STAT5B	Abcam	ab178941	Western blot/Immunoprecipitation
STAT5B	Abcam	ab235934	ChIP
TET2	Abcam	ab18950	Western blot/ChIP/Immunoprecipitation
PARP1	Abcam	ab191217	Western blot
c-PARP1	Abcam	ab32064	Western blot/Immunohistochemistry
FADD	Cell Signaling Technology	#2782	Western blot
FADD	Boster	A00237	Immunohistochemistry
CASP8	Cell Signaling Technology	#4790	Western blot
c-CASP8	Cell Signaling Technology	#9496	Western blot
CASP3	Cell Signaling Technology	#9662	Western blot
c-CASP3	Cell Signaling Technology	#9664	Western blot/Immunohistochemistry
Bcl-XL	Cell Signaling Technology	#2764	Western blot
Bcl2	Cell Signaling Technology	#15071	Western blot
H3K27me3	Cell Signaling Technology	#14820	ChIP
EZH2	Cell Signaling Technology	#5246	Western blot/ChIP/Immunoprecipitation
GAPDH	Zsbio	TA309157	Western blot

Supplementary Table 3. The primers sequences used for qRT-PCR,ChIP-qPCR and pyrosequencing assays.

qRT-PCR			
ATRX STAT5b TET2 FADD EZH2 GAPDH	Forward 5'-3'	Reverse 5'-3'	
	ACGGCGTTAGTGGTTGTCCTC	GCAGCATGTAGCTTCTCTCCTG	
	GCCACTGTTCTCTGGGACAATG	ACACGAGGTTCTCCTTGGTGAG	
	GCTTACCGAGACGCTGAGGAAA	AGAGAAGGAGGCACCACAGGTT	
	CTCCTGCGCGAGCTGCTCGC	GCCTTCTCCAATCTTTCCCAC	
	GACCTCTGTCTTACTTGTGGAGC	CGTCAGATGGTGCCAGCAATAG	
ChIP-qPCR			
ATRX promoter FADD promoter	Forward 5'-3'	Reverse 5'-3'	
	CACCGTCTGAGTCGGGTGTT	AGCGTCACCGTTTAGGGGAG	
	TGGAGCGGTGTCGCTTTTGT	TGCCCTCACATCTGTTGGTG	
pyrosequencing			
ATRX promoter	Forward 5'-3'	Reverse 5'-3'	Sequence to Analyze Distance To TSS
	TAGAGGATTGTTGTGATTAGTAGAG	TCAATTTAAATCTACTTCCTCTCATTACA	AAGGT ATTTATAGAT T -819

NEUROD1	194	0.00026	Transcription Factors	metastasis associated 1 family member 2
NEUROD2	192	0.00862	Transcription Factors	neuronal differentiation 6
ZNF696	191	5.9E-05	Transcription Factors	zinc finger protein 696
TFPI	190	1.1E-05	Transcription Factors	TF transcription factor 1
NF1D	190	7.4E-05	Transcription Factors	Kruppel-like factor 10
NFMS1	189	0.00015	Transcription Factors	insulin motif containing 62
SPF4	189	0.00002	Oncogenes / Translocated Cancer Genes	ELK-1, ETS-domain protein (ERF accessory protein 1)
IRF4	189	0.00043	Transcription Factors	zinc finger protein 254
TFH4	189	0.00121	Transcription Factors	TF transcription factor 4, p107/p130-binding
NFID1	188	7.4E-05	Transcription Factors	neurotrophin inducible 1, group D, member 1 // tyrosyl homone receptor, alpha
TCF22D3	188	0.00002	Transcription Factors	TCF22 domain family, member 3
HNF1B	187	1.3E-05	Transcription Factors	human hepatocyte nuclear factor 1, enhancer binding factor 1
HNF1C	187	0.00013	Homeodomain Proteins	gastrulation brain homeobox 2
ZNF43	187	5.2E-05	Homeodomain Proteins	zinc finger homeobox 3
GBPC2	187	1.3E-06	Transcription Factors	melanocyte sulfide oxidoreductase B2
STAT3B	186	0.00002	Transcription Factors	signal transducer and activator of transcription 58
STAT1L	186	1.3E-06	Transcription Factors	granulocyte-like transcription factor 1
ZNF91	185	0.00335	Transcription Factors	zinc finger protein 91
ZNF92	185	1.7E-05	Transcription Factors	bovhd box 42
FOI3	185	2.2E-05	Transcription Factors	FOI-like antigen 1
HPF25	184	0.00006	Transcription Factors	zinc finger protein 275
PKNOX1	184	0.00078	Homeodomain Proteins	PfKcN1containing 1 homeobox 1
AGL2	184	3E-05	Transcription Factors	gliosarcoma adenoma gene-like 2
TCF12	183	5.7E-05	Transcription Factors	transcription elongation factor A (98)-like 1
CTCF3	183	0.00004	Oncogenes / Translocated Cancer Genes / Protein Kinases	homeobox domain containing 3
ALX1B	181	0.00048	Homeodomain Proteins	ULK homeobox transcription factor 1, beta
AC7B	181	0.00002	Transcription Factors	CCNA4-NOT1 transcription complex subunit 3
ALX4	181	0.00014	Transcription Factors	Kruppel-like factor 4 (gap)
TP5	179	0.00002	Transcription Factors	schwingen transcription factor 1
BNA6	177	6.5E-05	Transcription Factors	myoblast X receptor alpha
MT1	177	0.00012	Transcription Factors	TATA element modulatory factor 1
NCOA2	177	0.00513	Oncogenes / Translocated Cancer Genes	NR2, coactivator 2
NCO1	177	0.00002	Transcription Factors	NR2, homeobox 1
FOH1	176	2.2E-05	Transcription Factors	bovhd box 1
HPF21	176	0.00005	Transcription Factors	zinc finger protein 251
RNF103	174	0.00015	Transcription Factors	ring finger protein 103
HPF24	174	1.4E-05	Transcription Factors	zinc finger protein 254
SMARCC2	174	0.00018	Transcription Factors	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2
TF43	173	0.00002	Transcription Factors	zinc finger domain 284
PBC2	173	0.00037	Homeodomain Proteins	pre-B-cell leukemia homeobox 2
TF13	173	0.00002	Transcription Factors	Kruppel-like factor 13 / protein-rich protein HNF1 subfamily 1-like
ZNF410	173	0.00031	Transcription Factors	zinc finger protein 410
TF40	173	0.00002	Transcription Factors	imidazole repeat containing 64
CRG1	172	8.8E-05	Transcription Factors	cellular response of EIA-stimulated genes 1
TFB11	171	8E-05	Transcription Factors	translating protein factor beta 1, reduced transcript 1
STAT4D1	171	5.5E-05	Transcription Factors	SEITA domain containing 1
SCAN2	171	0.00004	Transcription Factors	zinc finger and SCAN domain containing 20
KAT5A	171	5.8E-05	Transcription Factors	Kruppel-like factor 5
TF14	170	0.00005	Transcription Factors	mediator complex subunit 14
TF10	170	1.8E-06	Transcription Factors	general transcription factor subunit 1
TCF8BP1	170	0.00018	Transcription Factors	MEIS1 binding protein 1
MTB1	170	0.00002	Homeodomain Proteins	Meis homeobox 1
TPC	169	0.00002	Transcription Factors	nuclear transcription factor Y subunit gamma
TPC2	169	0.00006	Homeodomain Proteins	SCC homebox 4
GMPR1	168	0.00001	Transcription Factors	nuclear factor of activated T cells, cytoplasmic, calcium-ion-dependent 3
ATAC1	168	0.00002	Transcription Factors	activating transcription factor 7
ATF7	168	0.00002	Transcription Factors	nuclear respiratory factor 1
SPB3	168	0.00002	Transcription Factors	SRD transcription regulator family member 8
TF18	168	1.1E-05	Transcription Factors	CTA-like factor 3 (zinc domain transcription factor, epithelial-specific)
NF149	168	0.00011	Transcription Factors	zinc finger protein 149
ANK2	168	0.00002	Transcription Factors	ankyrin repeat containing 2
TFB4	168	0.00146	Transcription Factors	ankyrin repeat containing 2
ZNF412	168	0.00018	Transcription Factors	RG binding protein 142
TCF20	167	0.00002	Transcription Factors	zinc finger protein 142
ZNF430	167	0.00002	Transcription Factors	nuclear receptor co-repressor 1
ZNF431	167	0.00002	Transcription Factors	zinc finger, MYM-like 1
ZNF432	167	0.00002	Transcription Factors	zinc finger, MYM-like 2
ZNF433	167	0.00002	Transcription Factors	zinc finger, MYM-like 3
ZNF434	167	0.00002	Transcription Factors	zinc finger, MYM-like 4
ZNF435	167	0.00002	Transcription Factors	zinc finger, MYM-like 5
ZNF436	167	0.00002	Transcription Factors	zinc finger, MYM-like 6
ZNF437	167	0.00002	Transcription Factors	zinc finger, MYM-like 7
ZNF438	167	0.00002	Transcription Factors	

transcription factor associated 1 family member 2

nuclear differentiation 6

zinc finger protein 639

zinc finger protein 694

EZF transcription factor 1

Kruppel-like factor 1

isapante motif containing 62

LMK ETS-1 domain protein (SRF accessory protein 1)

zinc finger protein 254

nuclease response factor

EZF transcription factor 4; i07/a130-binding

nuclear receptor subfamily 1, group D, member 1 // thyroid hormone receptor, alpha

TSC22 domain family, member 3

human neuroendocrine virus type 1 enhancer binding protein 1

germination brain homeobox 2

zinc finger homeobox 3

methionine sulfoxide reductase B2

signal transducer and activator of transcription 58

granmyth-like transcription factor 1

zinc finger protein 51

kodhead box F2

PDS-like antigen 1

zinc finger protein 275

PRK-fam11 homeobox 1

pneumocystis adenoma gene-like 2

transcription elongation factor A-DNA-like 1

broadenomeid containing 3

LM homeobox transcription factor 1, beta

CORF-NOT transcription complex subunit 8

Kruppel-like factor 4 [gap]

activating transcription factor 5

retinoid X receptor alpha

TATA element modulatory factor 1

nuclear receptor coactivator 2

NKG homeobox 1

kodhead box H1

zinc finger protein 251

zinc finger protein 353

zinc finger protein 264

SARFOP-related, minus-associated, actin dependent regulator of chromatin, subfamily, member 2

zinc finger protein 430

zinc finger homeobox 2

Kruppel-like factor 13 // proteic-rich protein Haettl subfamily 1-like

zinc finger protein 410

transducing repeat containing 6A

cellular repressor of TPA-stimulated genes 1

transforming growth factor beta 1 inducible transcript 1

SERFA domain containing 1

zinc finger and SCAN domain containing 20

Klpvna methyltransferase 2A

mediator complex subunit 14

general transcription factor IIIH subunit 1

MED1 binding protein 1

Med homeobox 1

nuclear transcription factor Y subunit gamma

SK homeobox 4

nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 3

activating transcription factor 7

nuclear respiratory factor 1

SRD2 transcription regulator family member 8

E7A-like factor 3 (eta domain transcription factor, epithelial-specific)

zinc finger protein 148

a/b hydrolase/nuclease nuclear translocator 2

thyroid hormone receptor, alpha

GTF binding protein 1

zinc finger protein 142

nuclear receptor corepressor 1

zinc finger, MYM-type 3

TATA RNA polymerase II TATA box binding protein (TBP)-associated factor, 135kDa

RR domain containing 6

zinc finger protein 100

E7A-like factor 4 (eta domain transcription factor)

TSC22 domain family, member 1/DB

tubby ligand transcription factor

IRG2 and gfp2 2

zinc finger and homeodomains 3

bucarin rich repeat containing 14

isapante motif containing 15

transcription factor binding to GtSEI enhancer 3

solar cancer family 25, member 40

inhibitor of DNA binding 5, dominant negative helix-loop-helix protein

therapeutic embryonic stem

PHD finger protein 11

mediator complex subunit 27

chromosome 14 open reading frame 166

cyclin-dependent kinase 7

zinc finger, MYM-type 4

siah 1/3 ubiquitin protein ligase 2

basic leucine zipper nuclear factor 1

zinc finger protein 708

juxta-pro-oncogene

v-maf avian myeloblastosis/osteosarcoma oncogene homolog C

C/EBP-beta zinc finger, nucleic acid binding protein

ZCZ-family zinc finger C

small nuclear RNA activating complex polypeptide 1

SARFOP-related, minus-associated, actin dependent regulator of chromatin, subfamily, member 1

heat shock transcription factor 1

mediator complex subunit 1

deltor 2, E3 ubiquitin ligase

SMAD3 family member 3

general transcription factor IIA 1

zinc finger protein 544

NRE homeobox 1

chaperone containing TCP1, subunit 4 (delta)

PQZ and LM domain 1

TAF1 RNA polymerase II TATA box binding protein (TBP)-associated factor, 85kDa

wink-like-E3-associated protein 1

E7A-like factor 1 (eta domain transcription factor)

oncogenic homeobox 2

zinc-B-cell leukemia homeobox 4

WW domain binding protein 5

SPY box 15

mediator complex subunit 6

LM homeobox transcription factor 1, alpha

broadenomeid adjacent to zinc finger domain 18

zinc finger protein 613

zinc finger protein 218

general transcription factor IIIH subunit 3

coiled box 10

zinc-nit homeobox

paired fork containing 33

muscle enhancer factor 22

neurofibromin binding protein 5

zinc finger and BTB domain containing 33

zinc finger protein 248

zinc-like zinc finger 3

zinc finger, BTB domain containing 78

zinc finger, BTB domain family, member 4

metadendrin or mixed-leukemia leukemia, translocated to, 4

alkaline FBR E3 ubiquitin protein ligase 2

isapante motif containing 28

A kinase (PKA) anchor protein 17A

zinc finger protein 414

zinc finger and BTB domain containing 17

acylated related 48, cysteine oxidase

TAF1 RNA polymerase II TATA box binding protein (TBP)-associated factor, 100kDa

boudelle-like, DNA near protein

TATA box binding protein

olefinic non-sulfur assembly component 1

interferon regulatory factor 2

zinc finger protein 268A

zinc finger protein 362

peroxisome proliferator-activated receptor delta

brodmann-domain adjacent to zinc finger domain 28

279kDa zinc finger protein

proline homology, DSIF elongation factor subunit

zinc finger and double PHD finger, family 3

cytosolic regulatory element binding

DL, zinc finger and double PHD finger, family 3

methyl-CpG binding protein 2

nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor-4e 1

zinc finger protein 382

retinoic acid receptor, beta

PR domain containing 11

chromophan helicase DNA binding protein 2

CREB binding protein

kodhead box M1

TAT2 RNA polymerase II TATA box binding protein (TBP)-associated factor, 150kDa

enhancer of zeste 2 polycomb repressive complex 1 subunit

kodhead box K2

ring finger protein 648

CORF-NOT transcription complex subunit 3

zinc finger protein 648

v-maf avian myeloblastosis/osteosarcoma oncogene homolog K

AT rich interactive domain 3A (SBRTF-like)

thyroid hormone receptor interactor 13

nuclear receptor coactivator 4

PARAFIM family, member 4

BMT1 proto-oncogene, polycomb ring finger

E3-associated protein 1 (leucocyte cortical 2) alpha

siah 1/3 ubiquitin protein ligase 1

SMO family member 7

has family bHLH transcription factor 1

DAPD family member 5

lysine (Lys)-specific demethylase 38

chromophan helicase DNA binding protein 6

zinc finger RNA binding protein

X-box binding protein 2

zinc finger homeobox 4

zinc finger protein 331

zinc finger protein 79

growth factor independent 1 transcription repressor

leucine zipper, down-regulated in cancer 1

run-related transcription factor 1, translated to, 1 (ovdin R-related)

nuclear receptor subfamily 1, group 1, member 3

histohelical nucleases and subunit domains containing 1

zinc finger protein 135

ring finger protein 113A

kodhead box D3

nuclear factor related to hsp60 binding protein 1

(AMP responsive element binding protein

kodhead box N3

methyl-CpG binding domain protein 1

nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta

TEA domain family member 3

nuclear receptor 1

zinc finger protein 17

zinc finger protein 3

LM homeobox 1

zinc finger, ANS-type domain 3

zinc finger protein 114

zinc finger protein 337

zinc finger and BTB domain containing 25

(AMP responsive element binding protein-like 2

cytotoxic tumor-transferrin 1 interacting protein

neurofibromin-like 2

zinc finger protein 473

zinc finger, MYND-type 1

transcription factor 7

zinc finger protein 274

chromatin remodeler 3

nuclear transcription factor, X-box binding protein 2

SMO family member 5

testonin beta-cytoplasmic repeat containing 1

ring finger protein, LM domain interacting

sameiro domain containing 4

thyroid hormone receptor interactor 4

zinc finger and BTB domain containing 20

ets variant 5

small nuclear RNA activating complex polypeptide 2

SARFOP binding protein

zinc finger protein 37A

a/b hydrolase/nuclease nuclear translocator-like

REST corepressor 1

nuclear receptor subfamily 2, group F, member 6

zinc finger protein 4

E6 transcription factor for RE subunit 2

AT rich interactive domain 18 (SWI2-like)

general transcription factor IE subunit 2

transcription elongation factor 1

RNA methyltransferase 1

PCH and PRC2 interacting protein 1

T-cell acute lymphocytic leukemia 1

thyroid hormone receptor interactor 10

TAF12 RNA polymerase I TATA box binding protein (TBP)-associated factor, 180kDa

T-box binding protein 1

MTC-associated factor 3

TAF1 RNA polymerase I TATA box binding protein (TBP)-associated factor, 28kDa

zinc finger protein 32

LF3	1.27	0.00035	Transcription Factors	interleukin enhancer binding factor 3
KLF18	1.27	0.00031	Transcription Factors	Kruppel-like factor 18
ZNF184	1.27	0.00029	Transcription Factors	D site of albumin promoter (albumin D-box) binding protein
SMARCA1	1.26	0.00036	Transcription Factors	zinc finger protein 184
PLA1	1.26	0.00091	Transcription Factors	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a-like 1
SMAD1	1.26	0.00027	Transcription Factors	positive co-receptor binding protein A
TRIM4	1.26	0.00102	Transcription Factors	SMAD family member
ZNF18	1.26	0.00351	Transcription Factors	transcription factor A, mitochondrial
ZNF66	1.26	0.00122	Transcription Factors	zinc finger protein 18
PER3	1.25	0.00439	Transcription Factors	zinc finger, ANL-type domain 6
SMARCA1	1.25	0.01307	Transcription Factors	period circadian clock 3
TRAP2	1.24	0.00097	Transcription Factors	SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily a containing DEAD/H box 1
UBR4	1.24	0.00908	Transcription Factors	transcription factor AP-2 delta (activating enhancer binding protein 2 delta)
GTF3C1	1.24	0.01133	Transcription Factors	ubiquitin protein ligase E3 component n-recognin 4
ZNF14	1.24	0.00483	Transcription Factors	general transcription factor IIC subunit 1
BAF73	1.24	0.0095	Transcription Factors	v-rel avian reticuloendotheliosis viral oncogene homolog A
PCU3F1	1.24	0.00112	Transcription Factors	zinc finger protein 18
SMARCA1	1.23	0.00324	Transcription Factors	basic leucine zipper transcription factor, ATF-like 3
EDF3	1.23	0.04682	Transcription Factors	PCU class 3 homeobox 1
CBX1	1.23	0.00948	Transcription Factors	zinc finger protein 324
ATND2	1.23	0.00089	Transcription Factors	SWI/SNF-related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2
ZBTB32	1.23	0.01136	Transcription Factors	E2F transcription factor 3
YY1	1.23	0.00723	Transcription Factors	chromobox homolog 1
GTF2F2	1.22	0.00785	Transcription Factors	zinc finger and BTF domain containing 32
CHC1	1.21	0.00428	Transcription Factors	YY1 transcription factor
PAK1	1.21	0.00242	Transcription Factors	general transcription factor IF subunit 2
CT1	1.21	0.04182	Transcription Factors	chromodomain helicase DNA binding protein 1
PHRF1	1.20	0.00088	Transcription Factors	SdC-related, C/EBP activator protein
ATNL	1.20	0.01817	Transcription Factors	paired box 1
SFI	1.20	0.0074	Transcription Factors	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein
KZFS	1.20	0.01435	Transcription Factors	PHD and ring finger domains 1
NKX8E	1.20	0.00034	Transcription Factors	enophin 1
SAF73	1.20	0.00034	Transcription Factors	splicing factor 1
MBN2	1.20	0.01789	Transcription Factors	KARIC family zinc finger 5
ZNF400	1.20	0.00055	Transcription Factors	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, epsilon
ZNF219	1.20	0.00441	Transcription Factors	squamous cell carcinoma antigen recognized by T-cells 3
BRF1	1.20	0.00034	Transcription Factors	muscleblind-like splicing regulator 2
EDH1	1.20	0.00036	Transcription Factors	GLA binding protein p40
SALL1	1.19	0.01024	Transcription Factors	zinc finger protein 2
LMOT	1.19	0.00311	Transcription Factors	zinc finger protein 215
ZNF460	1.19	0.00385	Transcription Factors	BRF1, RNA polymerase II transcription initiation factor 80 kDa subunit
FOXB1	1.19	0.01413	Transcription Factors	enhancer of zeste 1 polycomb repressor complex 2 subunit
GTF2H2	1.19	0.00722	Transcription Factors	split-like transcription factor 1
ZNF408	1.19	0.00186	Transcription Factors	LM domain 7
AFGAP2	1.19	0.00145	Transcription Factors	zinc finger protein 460
MEIOS	1.19	0.00079	Transcription Factors	folded box 61
ZNF131	1.19	0.00679	Transcription Factors	general transcription factor IH subunit 2 /// general transcription factor IH subunit 2B (psuedogene) /// GTF2H2 family member C /// GTF2H2 family member C, copy 2
GTF3C1	1.19	0.00059	Transcription Factors	zinc finger protein 408
ZNF381	1.19	0.00851	Transcription Factors	ADP-ribosylation factor GTPase activating protein 2
NORC1	1.19	0.00871	Transcription Factors	mediator complex subunit 16
ZNF189	1.19	0.00445	Transcription Factors	zinc finger protein 133
KOBB	1.19	0.0046	Transcription Factors	general transcription factor IIC subunit 4
NFE2L1	1.19	0.00143	Transcription Factors	zinc finger protein 281
SL2	1.19	0.00028	Transcription Factors	NORC1 organizes homeobox
TAI3D	1.19	0.00976	Transcription Factors	zinc finger protein 189
BTBPL1	1.17	0.00184	Transcription Factors	retinoid X receptor beta
MTA1	1.17	0.02118	Transcription Factors	nuclear factor, erythroid 2-like 1
CHB6	1.16	0.00027	Transcription Factors	GLIM homeobox 2
TP53J1	1.16	0.00161	Transcription Factors	TAI3D RNA polymerase II, TATA box binding protein (TBP)-associated factor, 30kDa
SUP3H1	1.16	0.00284	Transcription Factors	basic transcription factor 3 pseudogene 11
ZNF405	1.15	0.00208	Transcription Factors	metastasis associated 1
ZNF416	1.15	0.00514	Transcription Factors	zinc finger protein 22
ZNF482	1.15	0.00293	Transcription Factors	tumor protein p53 inducible protein 13
ZNF86	1.15	0.04154	Transcription Factors	SPB homolog, histone chaperone
ZNF81	1.15	0.00384	Transcription Factors	zinc finger protein 605
ATF1	1.15	0.00242	Transcription Factors	zinc finger protein 416
PAZT	1.15	0.01112	Oncogenes / Translocated Cancer Genes / Homeodomain Proteins	zinc finger, RAN binding domain containing 2
BAZ1A	1.15	0.00951	Transcription Factors	zinc finger and BTF domain containing 6
MEIS3	1.15	0.00279	Transcription Factors	zinc finger protein 61
SOX11	1.14	0.00826	Transcription Factors	AF4/NR62 family member 1
ZNF169	1.14	0.01676	Transcription Factors	paired box 1
RBPR	1.14	0.00461	Transcription Factors	homeobox domain adjacent to zinc finger domain 1A
ZNF263	1.14	0.00854	Transcription Factors	Meis homeobox 2
BPV1	1.13	0.00853	Transcription Factors	zinc finger, MHM-type 5
UMAI1	1.13	0.01569	Transcription Factors	SPY type 13
ZSC4NR2	1.12	0.00147	Transcription Factors	zinc finger protein 169
TAH8	1.11	0.00089	Transcription Factors	retinoid/xenopus binding protein 9
FOXD1	1.11	0.01586	Transcription Factors	zinc finger protein 263
ZNF406	1.11	0.01032	Transcription Factors	regulatory factor X, 1 (influenza HLA class II expression)
ZNF207	1.11	0.00222	Transcription Factors	LM domain and actin binding 1
SMARCA1	1.10	0.00465	Tumor Suppressors	zinc finger protein 25
TFB	1.10	0.02539	Oncogenes / Translocated Cancer Genes	zinc finger and SCAN domain containing 22
BTB	1.10	0.04272	Transcription Factors	TAF4b, RNA polymerase II, TATA box binding protein (TBP)-associated factor, 105kDa
CAND1	1.09	0.04654	Transcription Factors	folded box D1
AFGAP2	1.09	0.01447	Transcription Factors	zinc finger, ANL-type domain 5
OSIS	1.09	0.04289	Transcription Factors	folded box N2
PP1R13L	1.09	0.01265	Transcription Factors	zinc finger protein 207
FOXD3	1.09	0.01218	Transcription Factors	SWI/SNF-related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
MYCP	1.09	0.01409	Transcription Factors	transcription factor EB
NCOA6	1.09	0.01208	Transcription Factors	basic transcription factor 3
ZBTB48	1.09	0.01891	Transcription Factors	coffee-associated and meckel-yeatan-disassociated 1
GLBP1	1.07	0.04891	Transcription Factors	Rho GTPase activating protein 35
SPS	1.05	0.02568	Homeodomain Proteins	chromobox homolog 2
				protein phosphatase 1, regulatory subunit 13 like
				folded box 13

				nuclear receptor coactivator 6
				zinc finger and BTF domain containing 48
				QA binding protein transcription factor alpha subunit
				SK homeobox 5

[illegible]

LGALS12	0.94	4.39E-01	---	lectin, galactoside-binding	chr11:63273899-63284246 (+) // 10 chr11a13	---	
STCL1	0.94	6.93E-01	0.602	serine/threonine kinase 1	chr19:12362314-12378931 (+) // 99.8 chr19a13.3	---	
PHLDA3	0.94	5.83E-01	---	pleckstrin homology-like 3	chr120:4348422-201438233 (-) // 9 chr12a131	---	
APAF1	0.94	6.02E-01	---	apoptosis activator	chr12:9039377-90129210 (+) // 88 chr12a2.3	Apoptosis // GenMAPP /// Apoptosis GenMAPP /// GenMAPP /// Apoptosis KEGG // GenMAPP	
ZMAT4	0.94	6.94E-01	---	zinc finger, matrix-type 4	chr8:40288112-40755343 (-) // 99.8 chr8a11.21	---	
PIHT	0.93	2.23E-01	---	phage histidine triad	chr5:5973794-61237124 (-) // 84 chr5a2.42	---	
MCAP1	0.93	5.88E-01	---	modulator of apoptosis 1	chr14:8364846-93851241 (-) // 43 chr14a32	---	
MAEL	0.93	9.01E-01	---	myeloid leukemia oncogene	chr1:16696519-16695455 (+) // 9 chr1a1a.1	---	
CHAC1	0.93	9.51E-01	---	CHAC glutathione-specific	chr15:41245890-41248709 (+) // 95 chr15a1.1	---	
POK2	0.93	2.46E-01	---	pyoxinyl dehydrogenase 4	chr17:46117285-46189732 (+) // 98 chr17a13.33	Krebs TCA Cycle // GenMAPP	
KRT18	0.92	4.79E-01	---	keratin 18, type I	chr12:53342910-53346694 (+) // 99 chr12a1.3	---	
TSCAP1	0.91	6.46E-01	---	tbl-like receptor adaptor	chr9:4393491-4617980 (-) // 95.2 chr9a13.3	---	
UPF2B	0.91	2.89E-01	---	ubiquitin specific peptidase	chr11:113669577-113746250 (-) // 1 chr11a2.3	---	
SNY1	0.91	5.54E-01	---	SWI domain containing 1	chr14:18183915-18221496 (-) // 98 chr14a3.4	---	
DIOC1	0.91	1.42E-01	---	death inducer-oligomer	chr20:63318965-61542416 (-) // 98 chr20a13.3	---	
APPL1	0.91	2.18E-01	---	adaptor protein, cholesteryl	chr15:7261853-73207496 (+) // 83 chr15a1.3	---	
RCOT1	0.90	3.66E-01	---	ret homologous family member	chr17:3269845-35525745 (+) // 9 chr17a11.2	---	
SET	0.90	2.75E-01	---	seamatin	chr3:18786689-18788032 (-) // 9 chr3a2.8	---	
DAP	0.90	3.34E-01	---	death-associated protein	chr5:10879425-10761339 (-) // 84 chr5a2.5.2	---	
PCCD10	0.89	5.34E-01	---	programmed cell death 10	chr3:107401686-107425984 (-) // 9 chr3a2.1	---	
BAO3	0.89	4.46E-01	---	BC1L-associated enhancer	chr10:121415981-121437798 (+) // chr10a5.5-5a6.2	---	
EYAZ	0.89	2.63E-01	---	EYA transcriptional coactivator	chr20:6618647-65817490 (-) // 98 chr20a1.1	---	
ZNF35C	0.89	1.64E-01	---	zinc finger protein 35C	chr17:40190249-40190702 (-) // 19 chr17a12.2	---	
COPBP2	0.89	1.66E-01	---	casein 8 associated protein	chr6:90272736-90584148 (+) // 82 chr6a1.5	---	
COSB	0.88	3.87E-01	---	COSB molecule	chr4:13778914-13804486 (+) // 82 chr4a2.5	PYRIDNUCSAL -PWY // HumanCyc /// PYRIDNUCSAL -PWY // MetaCyc	
MIF	0.88	1.06E-01	---	mitochondrial fusion factor	chr2:228139473-228222453 (+) // 9 chr2a26.3	---	
USEX1	0.87	1.39E-01	---	ubiquitin conjugating enzyme	chr4:33696575-36761552 (+) // 84 chr4a2.4	---	
MAPT	0.87	1.42E-01	---	microtubule associated protein	chr17:43971829-44103471 (+) // 83 chr17a2.1	---	
DAB2IP	0.85	4.58E-01	---	DAB2 interacting protein	chr15:124527405-124547809 (+) // 9 chr15a2.11-53.3	---	
PKCA	0.85	3.41E-01	---	protein kinase C, alpha	chr17:54832385-54833325 (+) // 98 chr17a22-52.2	Calcium regulation in cardiac cells // GenMAPP /// G Protein Signaling // GenMAPP /// Smooth muscle contraction // GenMAPP /// Wnt signaling // GenMAPP	
IL7	0.84	4.24E-01	0.4	interleukin 7	chr4:123373234-123377462 (-) // 9 chr4a2.6-27	Inflammatory Response Pathway // GenMAPP	
TMEM109	0.83	1.02E-01	---	transmembrane protein 109	chr11:469681676-60690913 (+) // 98 chr11a12.2	---	
ACHV1B	0.83	2.97E-01	---	acholin A receptor subunit B	chr15:52549450-52589473 (+) // 98 chr15a2.3	---	
JA2	0.83	5.14E-01	---	Janus kinase 2	chr9:5065804-5068158 (+) // 78.23 chr9a24	---	
RAPI1	0.82	1.13E-01	0.421	Raf-1 serine-threonine	chr12:12079464-12531279 (-) // 13.3 chr12a2.5	MAPK Cascade // GenMAPP	
TNCD1	0.79	3.55E-01	---	TMZ domain containing 1	chr1:62163025-62165517 (-) // 32.4 chr1a1.3	---	
CIL5	0.78	6.94E-02	---	cullin 5	chr11:107879549-107878739 (+) // 9 chr11a2.3	---	
TNFRSF11A	0.78	8.56E-02	---	tumor necrosis factor receptor	chr18:59982547-60053502 (+) // 88 chr18a2.1	---	
IL4	0.77	2.22E-01	---	interleukin 4	chr5:12309677-130202010 (+) // 9 chr5a2.1	Inflammatory Response Pathway // GenMAPP	
XPA	0.76	9.32E-02	---	xeroderma pigmentosum	chr9:100437181-100459600 (-) // 3 chr9a22.3	---	
TNMD3	0.76	1.79E-01	---	translocase of inner mitochondrial	chr19:5996501-59965201 (+) // 14 chr19a1.2	---	
DAPK3	0.76	1.58E-01	---	death-associated protein	chr9:90112795-9033543 (+) // 88 chr9a21.33	---	
DDIT4	0.75	1.91E-01	---	DNA damage inducible 4	chr10:1602661-16057981 (+) // 98 chr10a2.1	---	
KIAA041	0.74	9.59E-02	---	KIAA041	chr5:145303396-14133717 (+) // 7 chr5a21.3	---	
TGF	0.73	5.01E-02	---	tumor necrosis factor	chr6:288762-388590 (+) // 21.82 chr6a21.3	Apoptosis // GenMAPP /// Apoptosis GenMAPP /// GenMAPP /// Apoptosis KEGG // GenMAPP /// Matrix Metalloproteinases // GenMAPP /// TGF Beta Signaling Pathway // GenMAPP	
TRE	0.73	1.12E-01	---	trichostatin growth factor	chr4:175962-1815981 (+) // 76.5 chr4a2.6.3	GLUCONOLIPER -PWY // HumanCyc	
TREB3	0.70	1.03E-01	---	troubled pseudokinase 3	chr20:261674-373719 (+) // 95.29 chr20a13-512.2	---	
RLJL1	0.69	1.10E-01	---	RLJL-related protein A3	chr15:86252324-86262381 (-) // 89 chr15a24.3	Apoptosis KEGG // GenMAPP	
ZNF35B	0.68	7.26E-02	---	zinc finger protein 35B	chr2:180207296-18044095 (-) // 8 chr2a31.2-531.3	---	
TNFRSF25	0.68	1.51E-01	---	tumor necrosis factor receptor	chr15:821211-4526225 (-) // 87.75 chr15a2	Apoptosis // GenMAPP	
ATN	0.65	6.75E-02	---	apoptosis enhancing nucle	chr15:89169755-89175512 (+) // 91 chr15a26.1	---	

Supplementary Table 6. The Pearson correlation among ATRX and genes in apoptotic signaling pathway.

	R	P value	P value summary
ATRX vs. ATM	0.41	<0.0001	****
ATRX vs. BCL2L1	-0.30	<0.0001	****
ATRX vs. CASP8	-0.03	0.7512	ns
ATRX vs. CDKN1A	-0.16	0.038	*
ATRX vs. EP300	0.42	<0.0001	****
ATRX vs. FADD	-0.47	<0.0001	****
ATRX vs. FAS	-0.13	0.0961	ns
ATRX vs. FOXO3	0.44	<0.0001	****
ATRX vs. HRAS	-0.40	<0.0001	****
ATRX vs. MSH6	0.32	<0.0001	****
ATRX vs. PRKDC	0.55	<0.0001	****
ATRX vs. SMAD3	0.33	<0.0001	****
ATRX vs. TNFSF10	-0.11	0.1653	ns