

Supplementary file 1

Comprehensive pan-cancer analysis and experimental validation of mitotic arrest defective 2-like 1 (MAD2L1) in colorectal cancer

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Table S1 GTEx Statistical description indicators for tissues included in this study.

x	group	n	min	max	median	iqr	q1	q3	mean	sd	se
ACC	Tumor	79	0.16272565 3	6.41746099 4	3.36061711 2	1.80246057 6	1.98715677 4	3.78961735	3.01420141 9	1.17253679 3	0.13192069 6
BRCA	Norma I	113	0.82293404 8	4.29682445 9	2.23431737	0.88238084 5	1.69019357 8	2.57257442 3	2.17468247 1	0.63225522	0.05947756 8
BRCA	Tumor	111 3	0.65562660 1	7.39517507 7	3.80004049 6	1.43833523 8	3.14641084 3	4.58474608	3.85140782 9	0.98111260 8	0.02940839 2
CHOL	Norma I	9	0.34050530 1	0.73439530 9	0.49385224 8	0.24175902 9	0.36221737 7	0.60397640 6	0.50597194	0.14001540 4	0.04667180 1

CHOL	Tumor	35	1.72848653 3	4.83945576 5	2.68407812 9	0.82382701 6	2.37681353 8	3.20064055 4	2.86129336 1	0.79356215	0.13413648 6
COA D	Norma I	41	1.73976171 1	4.49538177 7	3.22546003 7	0.84699530 5	2.83600489 5	3.6830002	3.23780461 3	0.61137256 4	0.09548035 3
COA D	Tumor	480	1.19105724	6.89053302 8	4.92949140 2	1.02919390 5	4.39163196 9	5.42082587 4	4.85045014 9	0.83339956 6	0.03803931 2
READ	Norma I	10	2.98480806 2	4.84398384 4	3.63682503 2	0.94690947 9	3.36909855 2	4.31600803 1	3.80431105 4	0.62172692 6	0.19660731 7
READ	Tumor	167	2.07597752 2	6.42074175 9	4.83781208 2	1.08260316 8	4.25484281 3	5.33744598	4.77965934 4	0.79188050 7	0.06127755 3

Table S2 Statistical description of paired samples.

x	group	n	min	max	median	iqr	q1	q3	mean	sd	se
BLCA	Norma I	19	0.86385917 9	4.25237024 1	1.96547032	1.16675404 3	1.58767244 1	2.75442648 3	2.25799398 2	0.90833177 9	0.20838560 2
BLCA	Tumor	19	2.68353926 5	5.99264835 2	3.84774641 7	1.19339103 3	3.40985976	4.60325079 2	4.04381324 3	0.91465413 8	0.20983605
BRCA	Norma I	11 3	0.82293404 8	4.29682445 9	2.23431737	0.88238084 5	1.69019357 8	2.57257442 3	2.17468247 1	0.63225522	0.05947756 8
BRCA	Tumor	11 3	1.03421571 5	5.93485614 1	3.80004049 6	1.58271047 6	3.10641532 7	4.68912580 3	3.87196574 2	1.04038876	0.09787154 2
CESC	Norma I	3	1.28332916 8	2.37526190 2	1.78379188 2	0.54596636 7	1.53356052 5	2.07952689 2	1.81412765 1	0.54659808 6	0.31557855 2
CESC	Tumor	3	4.26650921 7	5.99488741 8	4.28904504 5	0.86418910 1	4.27777713 1	5.14196623 1	4.85014722 7	0.99143812	0.57240706 5

CHOL	Norma I	8	0.34050530 1	0.73439530 9	0.49159482 8	0.25750885 4	0.36204898 3	0.61955783 7	0.50651624 7	0.14967258 3	0.05291724 9
CHOL	Tumor	8	2.35284325 4	4.83945576 5	3.16485373 7	1.32243544 2	2.55272902 6	3.87516446 8	3.31772056	0.90832633 1	0.32114185 4
COAD	Norma I	41	1.73976171 1	4.49538177 7	3.22546003 7	0.84699530 5	2.83600489 5	3.6830002	3.23780461 3	0.61137256 4	0.09548035 3
COAD	Tumor	41	2.21288056 6	6.16284244 7	4.84826738 7	1.09309808 1	4.42631172 5	5.51940980 7	4.75490898 4	0.95894546 3	0.14976212
ESCA	Norma I	8	0.54468320 5	3.84031215 8	2.20889174 1	1.77842808 1	1.23067788	3.00910596	2.18241333 6	1.16593030 9	0.41221861 4
ESCA	Tumor	8	3.53389968 9	5.18899823 1	4.30803099 9	0.99823807 6	3.95405038 8	4.95228846 3	4.38799884 4	0.61559531 4	0.21764581
HNSC	Norma I	43	0.73022692 2	3.74591494 9	2.88248654 5	1.09026044 6	2.10077584 8	3.19103629 4	2.64205136 8	0.79562673 7	0.12133194
HNSC	Tumor	43	2.93719371 1	5.21366222 9	4.12580812 3	0.93861065 9	3.62545938	4.56407003 9	4.09713369 8	0.67257827 3	0.10256722 5
KICH	Norma I	24	1.16844949 2	3.00640575 1	1.58734109 7	0.46344418 6	1.46509931 4	1.92854349 9	1.72866129 8	0.42374696 6	0.08649698 7
KICH	Tumor	24	0.76773953 6	4.21253821 2	1.81244058 9	1.11698446 9	1.30845726 1	2.42544173	2.02719641 3	0.98997250 5	0.20207729 1
KIRC	Norma I	72	0.77635670 1	4.20861870 1	1.48909569 9	0.54041769 6	1.30099546 7	1.84141316 3	1.59114773 3	0.51861210 2	0.06111902 2
KIRC	Tumor	72	1.09511425 9	4.33204908 4	2.43067110 7	0.61098335 9	2.14347454 7	2.75445790 6	2.49001558 1	0.54424987 6	0.06414046 3
KIRP	Norma I	32	0.95337699 9	2.63431446	1.30325664 8	0.34251252 8	1.12883103 2	1.47134356	1.36637620 8	0.37878695	0.06696070 5

KIRP	Tumor	32	0.38416035 4	3.93442214 3	2.00708573 8	1.08893792 5	1.37883772 4	2.46777564 9	2.07294612 8	0.89889773 7	0.15890417 1
LIHC	Norma I	50	0.20075543 2	1.61692224 2	0.56076367 2	0.29882904 9	0.40542057 5	0.70424962 4	0.61169149 3	0.29261505 1	0.04138201 7
LIHC	Tumor	50	0.20389022 7	4.50506520 8	1.96894570 3	1.18468798 4	1.52451333 7	2.70920132 2	2.11748750 6	0.99987456 3	0.14140361 7
LUAD	Norma I	58	0.82692468 3	2.42974985 1	1.54141461 2	0.38214087 6	1.34269755 4	1.72483843	1.56591289 5	0.32440290 5	0.04259618 8
LUAD	Tumor	58	1.23713537 4	6.13225808 2	3.49015602 2	1.32874390 9	2.83927480 3	4.16801871 1	3.49011997 9	1.09903569	0.14431045 6
LUSC	Norma I	49	0.79152237 8	3.05642745 9	1.57240464 7	0.68369377 9	1.20683073 7	1.89052451 6	1.58756982 2	0.51121045 7	0.07303006 5
LUSC	Tumor	49	1.49881251 6	6.21608619 7	4.61116647 7	1.24598203 2	3.91563562 3	5.16161765 6	4.45564461	0.99099538 8	0.14157077
PAAD	Norma I	4	1.69447907 9	3.16552609 7	1.98795237 6	0.47491802 7	1.86100591 6	2.33592394 2	2.20897748 2	0.65513476 8	0.32756738 4
PAAD	Tumor	4	2.45677987	3.58353111 8	2.72637078 2	0.46072798 6	2.56945296 7	3.03018095 3	2.87326313 8	0.49986242 1	0.24993121
PCPG	Norma I	3	0.78810099 8	1.47014636 7	1.13986236 8	0.34102268 5	0.96398168 3	1.30500436 8	1.13270324 4	0.34107903 9	0.19692207 5
PCPG	Tumor	3	1.71510263 6	3.08635918 2	1.90919706 3	0.68562827 3	1.81214985	2.49777812 2	2.23688629 4	0.74203861 3	0.42841619 3
PRAD	Norma I	52	0.58390413 6	3.61536921 1	2.09796182 8	0.75709374 6	1.73098591 7	2.48807966 3	2.07709794 9	0.65280972 3	0.09052842
PRAD	Tumor	52	0.37640152 7	4.96557190 4	2.34147440 5	0.64695862 8	1.99369091 7	2.64064954 5	2.37287713 4	0.651526	0.0903504

READ	Norma I	9	2.98480806 2	4.84398384 4	3.65289945 4	0.97925766 1	3.36625226 4	4.34550992 4	3.85171923 6	0.63998253 1	0.21332751
READ	Tumor	9	3.62927501 1	6.34904852 1	4.67790846 6	0.89348340 6	4.36453041 1	5.25801381 8	4.87482187	0.84287013 1	0.28095671
SARC	Norma I	2	1.29719141 7	2.16259676 6	1.72989409 1	0.43270267 5	1.51354275 4	1.94624542 9	1.72989409 1	0.61193399 1	0.43270267 5
SARC	Tumor	2	1.93489387 4	4.40952671 3	3.17221029 3	1.23731641 9	2.55355208 4	3.79086850 3	3.17221029 3	1.74982966 1	1.23731641 9
SKCM	Norma I	1	4.07309184 8	4.07309184 8	4.07309184 8	0	4.07309184 8	4.07309184 8	4.07309184 8		
SKCM	Tumor	1	4.33256473 1	4.33256473 1	4.33256473 1	0	4.33256473 1	4.33256473 1	4.33256473 1		
STAD	Norma I	27	0.66530180 4	3.05003146 1	1.76638314 1	1.02188107 3	1.46638221 5	2.48826328 7	1.91167754 8	0.68262953 4	0.13137211 5
STAD	Tumor	27	2.17606740 6	5.32999182 3	4.04728535 4	1.30298798	3.13611978 2	4.43910776 3	3.85315082 5	0.91725487 2	0.17652578 2
THCA	Norma I	59	0.63580081 7	3.04421923 7	1.54818998 9	0.37598268 5	1.41594697 1	1.79192965 5	1.67407093 5	0.46354662 6	0.06034863
THCA	Tumor	59	0.40664550 8	2.92582856 3	1.75736467 2	0.48935091 8	1.47006121 7	1.95941213 5	1.74335454 2	0.48263950 3	0.06283431 1
THY M	Norma I	2	3.48679158 9	5.40807663 7	4.44743411 3	0.96064252 4	3.96711285 1	4.92775537 5	4.44743411 3	1.35855368 6	0.96064252 4
THY M	Tumor	2	5.49901669 7	6.19358449 6	5.84630059 7	0.3472839	5.67265864 7	6.01994254 6	5.84630059 7	0.49113360 1	0.3472839
UCEC	Norma I	23	1.34556669 5	3.50542096 1	2.11686375 8	0.98956117 6	1.65307091 1	2.64263208 8	2.21087987 8	0.61680565 7	0.12861287

Table S3 Forest plot and Cox regression analyses.

Characteristics	Total(N)	HR(95% CI)
ACC	79	2.218 (1.461 - 3.367)
BRCA	1086	1.171 (1.003 - 1.367)
HNSC	503	1.189 (1.012 - 1.397)
KICH	64	4.865 (2.320 - 10.202)
KIRP	290	2.609 (1.764 - 3.858)
LGG	530	1.516 (1.309 - 1.756)
LIHC	373	1.407 (1.196 - 1.656)
LUAD	530	1.274 (1.123 - 1.446)
MESO	86	2.490 (1.768 - 3.507)
PAAD	179	1.489 (1.142 - 1.941)
PCPG	184	3.025 (1.049 - 8.724)
PRAD	501	2.738 (1.277 - 5.872)
READ	166	0.579 (0.380 - 0.881)
SARC	263	1.360 (1.107 - 1.671)
THYM	119	0.474 (0.264 - 0.852)
COADREAD	643	0.649 (0.457 - 0.921)

Table S4 MAD2L1 promoter DNA methylation levels in 22 cancer types vs. normal tissues.

	BLC	BRC	CHO	COA	CES	ESC	GB	HNS	KIRC	KIRP	LIHC	LUA	LUS	PAA	PR	PCP	REA	SAR	STA	THC	THY	UCE
	A	A	L	D	C	A	M	C				D	C	D	AD	G	D	C	D	A	M	C

P 值	1.80 E-03	2.64 E-01	6.84 E-02	1.87 E-01	2.96 E-01	5.71 E-05	8.61 E-01	8.12 E-02	3.36 E-06	9.64 E-02	7.76 E-01	9.91 E-01	<1E- 12	1.31 E-02	1.1 3E- 06	6.37 E-01	5.12 E-01	6.07 E-01	8.51 E-01	2.31 E-02	2.42 E-01	1.75 E-02
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Table S5 The correlation between MAD2L1 expression and mRNAs modification regulators. The full dataset with all individual data points is provided as a separate Excel file.

TYPE	m1A_writer-1	m1A_writer-2	m1A_writer-3	m1A_writer-4	m1A_reader-1	m1A_reader-2	m1A_reader-3	m1A_reader-4
GENE	TRMT61A	TRMT6	TRMT10C	TRMT61B	YTHDC1	YTHDF1	YTHDF2	YTHDF3
ACC	0.49679008	0.645941808	0.617645374	0.672407282	0.744139031	0.661931455	0.721133089	0.664573337
BLCA	0.188656432	0.504832331	0.496744107	0.564853591	0.362729803	0.445137135	0.500277056	0.433424892
BRCA	0.05918221	0.452707776	0.429755855	0.303171401	0.269941434	0.409871778	0.327320527	0.37229154
CESC	0.221719846	0.400035968	0.376299012	0.550486445	0.560667923	0.423752174	0.489847064	0.47617778
CHOL	0.153627225	0.233405585	0.07230967	0.351628841	0.246396793	0.231355943	0.170174394	0.10713958
COAD	0.040031	0.402280506	0.771837637	0.587017342	0.422661554	0.303633966	0.558289921	0.520679468
COADREAD	0.011656996	0.405782871	0.76359388	0.572204695	0.412180295	0.290610989	0.555086404	0.497772229

Table S6 EPIC-based correlation analysis of MAD2L1 expression and TME immune cell fractions. The complete dataset is available in Supplementary File 2.

cancer	infiltrates	rho	p	adj.p
ACC (n=79)	B cell_EPIC	0.072676346	0.541174145	0.708648832
BLCA (n=408)	B cell_EPIC	-0.057017045	0.275297895	0.459403362
BRCA (n=1100)	B cell_EPIC	0.124611307	8.17757E-05	0.000590111
BRCA-Basal (n=191)	B cell_EPIC	-0.033764105	0.658275682	0.793633113
BRCA-Her2 (n=82)	B cell_EPIC	-0.080688199	0.500451603	0.674851405

BRCA-LumA (n=568)	B cell_EPIC	0.062130495	0.158349573	0.316462095
BRCA-LumB (n=219)	B cell_EPIC	0.105066411	0.146959957	0.301138208
CESC (n=306)	B cell_EPIC	0.027799298	0.645035843	0.786524041
CHOL (n=36)	B cell_EPIC	-0.181931439	0.295564311	0.480899885
COAD (n=458)	B cell_EPIC	-0.11508185	0.056642275	0.145558107

Table S7 Correlation analysis between ICP gene and MAD2L1 expression in pan-cancer cohorts.

	CD274	CTLA4	HAVCR2	LAG3	PDCD1	PDCD1LG2	TIGIT	SIGLEC15
ACC	0.797760075	0.049281746	0.384125559	0.241084153	0.125233262	0.303804043	0.092745961	0.278910409
BLCA	5.22259E-10	0.002755692	0.000206739	6.04437E-07	0.01861306	1.00507E-05	0.000501244	1.77206E-11
BRCA	0.002317364	1.75323E-06	0.026981732	7.62928E-09	0.178663541	0.000349977	0.000107252	1.61955E-27
CESC	0.193111529	0.744920956	0.813256857	0.930768802	0.676632287	0.331906244	0.776583471	0.413576539
CHOL	0.229957585	0.139663209	0.706267224	0.385157098	0.284268363	0.601740767	0.410553205	0.507687496
COAD	0.002398937	0.392649919	0.048190653	0.244743932	0.925932669	0.013379775	0.218492647	0.003464433
COADREAD	0.000166429	0.23716854	0.010477567	0.398010766	0.558972553	0.006858172	0.373462016	0.001544852
DLBC	0.100992017	0.158084702	0.307405886	0.711662197	0.813686374	0.090392617	0.035713799	0.936422318
ESCA	0.263462937	0.66554297	0.579005855	0.540107972	0.768302715	0.844780298	0.712239266	0.465438861
GBM	4.42168E-07	0.00424124	0.002544464	0.107550625	0.504975173	1.08339E-06	0.00992482	0.120925066
HNSC	0.101609263	0.132015278	0.037622837	0.059230153	0.293947912	0.668691929	0.513990575	0.061725597
KICH	0.015364854	0.948386201	0.376801965	0.535169327	0.427413696	0.77079666	0.526051796	7.41714E-08
KIRC	0.12171873	0.000126345	0.005934842	0.000189679	0.001565108	6.66153E-13	3.96497E-08	1.95457E-06
KIRP	0.000248214	0.419400243	0.995446267	0.163974635	0.04495845	4.33172E-06	0.02278784	0.160767538
LAML	0.38827888	0.002201359	0.576771265	0.000522719	0.01297377	0.494067811	0.003984401	0.018991114
LGG	0.311512451	0.008725252	0.019853345	3.26902E-11	0.005900525	0.001339359	0.008369495	0.002769103
LIHC	2.43344E-06	1.16337E-12	4.9952E-13	8.61884E-08	6.50199E-11	0.002618981	9.56992E-11	0.55259481

LUAD	6.40446E-10	0.054442903	0.000263421	6.13661E-06	0.003122121	4.02849E-09	0.069815055	0.003369585
LUSC	0.02323213	0.036979045	0.083853097	0.619535171	0.034405483	0.028961731	0.050704291	0.006094766
MESO	0.032189263	0.058148841	0.141794696	0.597893641	0.153604759	0.04304438	0.102481072	0.757263288
OV	0.267548068	0.069623977	0.602386885	0.032817575	0.41997524	0.083248319	0.258515813	0.04397985
PAAD	0.000503873	0.165325264	0.804035775	0.291993861	0.077285448	0.191470194	0.26528879	0.536181046
PCPG	3.01842E-10	0.193569755	0.223378131	0.184613378	0.954799382	0.222495908	0.004837905	0.000733291
PRAD	0.01002704	0.182645918	8.4869E-06	4.71595E-06	0.559730152	1.45978E-05	0.001114979	1.24838E-06
READ	0.006571836	0.363187613	0.834334654	0.420514969	0.243965754	0.397876026	0.687732898	0.146135373
SARC	0.059206485	0.939816045	0.143296095	0.869093264	0.083236715	0.381356626	0.352931685	0.005549856
SKCM	0.024828108	0.46638625	0.303273663	0.061525107	0.004441063	0.00162385	0.635206639	0.007463809
STAD	2.62739E-07	0.000361023	0.170339224	0.005299639	0.787609793	0.450668557	0.656694691	0.093709587
TGCT	0.016875479	1.27054E-05	0.072940859	0.00016651	2.93901E-07	0.000290037	0.000245069	1.3677E-05
THCA	7.73104E-16	1.92456E-08	1.77637E-08	0.172059276	0.264162443	8.51022E-12	3.15698E-08	0.159319138
THYM	0.035929933	0.000622697	0.0019342	2.61216E-06	1.96513E-10	0.128993671	0.001255074	0.09455874
UCEC	2.61158E-07	0.47257114	3.92823E-05	0.007953595	0.024588822	1.17763E-09	0.002828342	0.097764576
UCS	0.836867693	0.617599053	0.580827587	0.260218534	0.206046192	0.516488577	0.451949354	0.336608275
UVM	0.025364918	0.098174319	0.029560851	0.205192508	0.086461667	0.029575589	0.108461788	0.921321508

Table S8 The correlation between MAD2L1 expression and genes linked to copper-induced apoptosis in various cancers.

Gene	MTF1	PDHB	PDHA1	DLAT	DLD	LIPT1	LIAS	FDX1
ACC	1.84604E-12	8.35048E-07	0.000916507	3.78328E-10	7.43677E-10	0.000825979	2.55165E-07	0.001400552
BLCA	1.25647E-21	1.19203E-13	3.77755E-31	1.7436E-36	2.99261E-27	0.172212051	0.002276437	0.002473172
BRCA	2.71856E-17	0.248302225	4.11502E-54	1.8618E-50	7.25653E-47	0.000245044	0.374186196	0.13737137
CESC	2.93509E-10	9.83188E-18	2.48251E-09	7.09634E-20	1.26959E-18	1.93835E-08	1.77081E-15	0.010745438
CHOL	0.492412467	0.609638971	0.419118541	0.610394806	0.698401532	0.526636176	0.110552298	0.616235719

COAD	3.41623E-06	1.93944E-36	5.22404E-09	4.37047E-56	2.52831E-52	1.54737E-27	5.42923E-35	4.59904E-32
DLBC	0.055029689	4.45895E-05	0.013087901	1.83374E-08	9.18336E-06	0.656996398	0.010513507	0.917821568
ESCA	0.142345458	7.16442E-05	8.16486E-08	3.25797E-05	8.39027E-06	0.000645042	2.07048E-05	0.585186546
GBM	0.152937082	2.58252E-06	8.15777E-05	0.002157199	0.233618979	0.006474866	0.003230115	0.05523784
HNSC	0.00562969	1.53808E-26	6.72275E-30	8.37749E-16	2.20185E-29	1.15781E-28	2.41165E-20	7.76511E-08
KICH	0.517946643	0.422797763	0.05430361	0.405899376	0.339176344	0.29061293	0.614731311	-0.016591159
KIRC	5.29093E-24	6.2399E-18	1.34585E-08	5.36638E-35	1.44498E-34	1.07912E-11	1.06074E-14	1.27894E-15
KIRP	2.6229E-18	3.18152E-05	0.916024512	2.69856E-15	0.000110051	6.95454E-06	0.00069361	0.000552862
LAML	0.601680191	6.52546E-09	1.07773E-06	2.13521E-14	7.20997E-10	0.001184195	6.52391E-06	0.007253607
LGG	2.92265E-10	0.001388	9.85235E-14	7.64816E-15	1.46915E-20	6.38751E-07	1.59902E-07	1.30175E-16
LIHC	5.42569E-20	4.42601E-10	1.416E-11	1.09481E-16	2.6107E-06	5.16686E-14	0.008456351	4.52544E-05
LUAD	0.405718226	1.22063E-05	1.53769E-06	1.87525E-26	9.47594E-28	0.409847712	0.250116153	0.285939476
LUSC	0.334163877	7.15268E-12	2.15042E-14	6.85793E-16	3.20672E-22	1.22461E-21	1.30348E-11	1.38942E-08
MESO	0.0005039	0.846138006	0.00035315	0.007214232	0.008822096	0.911330304	0.017921738	0.986384974
OV	0.603554021	0.001967248	0.000482154	0.001353666	0.001453715	0.418449257	0.001319289	0.075497367
PAAD	4.89787E-05	5.38571E-05	3.99009E-15	7.13514E-15	1.8253E-09	0.03791955	3.68704E-05	0.002448039
PCPG	4.66566E-07	3.32718E-16	3.63729E-06	6.12964E-26	9.58562E-18	1.37048E-07	2.39514E-19	0.903554342
PRAD	4.23614E-25	6.90115E-35	1.38088E-30	1.34033E-51	8.24391E-52	0.000200508	6.42595E-16	7.18517E-23
READ	2.51959E-05	9.57539E-13	1.39584E-07	1.65109E-20	2.9644E-13	2.12736E-09	2.93059E-18	2.93545E-05
SARC	6.41133E-11	0.003428171	1.51346E-11	1.6721E-09	2.55569E-08	0.199149213	0.003125177	0.009582812
SKCM	3.93142E-33	5.30498E-33	7.15185E-42	4.54556E-61	2.90142E-64	1.63775E-37	5.4365E-34	3.5958E-36
STAD	3.93142E-33	5.30498E-33	7.15185E-42	4.54556E-61	2.90142E-64	1.63775E-37	5.4365E-34	3.5958E-36
TGCT	8.4373E-07	5.59301E-29	1.18071E-24	9.24963E-43	1.1642E-21	0.01044733	0.066955984	2.78316E-08
THCA	1.1965E-26	2.24801E-18	0.022505936	1.70401E-33	7.28872E-22	0.026354709	1.97067E-12	0.000595264
THYM	0.198492734	1.47824E-11	0.877988556	2.27852E-05	5.32584E-05	0.861041669	0.936867887	1.36141E-08

UCEC	2.92977E-46	1.48708E-49	1.68664E-29	1.3596E-103	8.8389E-101	1.7062E-24	1.89354E-44	5.09191E-69
UCS	0.000283693	0.221761523	0.316235774	0.000672706	5.45947E-07	0.646679992	0.000908401	0.892228742
UVM	5.74414E-11	3.72572E-11	6.56309E-17	1.25074E-19	8.45133E-17	4.8851E-13	1.14344E-14	3.34468E-16

Table S9 CRC-specific miRNA candidates targeting MAD2L1 predicted by the miRwalk, DIANA-microT, miRcode, and miRDIP databases.

miRcode	miRwalk	DIANA-microT	mirDIP
miR-93/93a/105/106a/291a-3p/294/295/302abcde/372/373/428/519a/520be/520acd-3p/1378/1420ac	hsa-let-7a-5p	hsa-miR-4704-3p	hsa-let-7a-2-3p
miR-135ab/135a-5p	hsa-let-7a-2-3p	hsa-miR-6780a-3p	hsa-let-7a-3p
miR-138/138ab	hsa-let-7b-5p	hsa-miR-548	hsa-let-7a-5p
miR-145	hsa-let-7b-3p	hsa-miR-548h-3p	hsa-let-7b-3p
miR-150/5127	hsa-let-7c-5p	hsa-miR-3148	hsa-let-7b-5p
miR-17/17-5p/20ab/20b-5p/93/106ab/427/518a-3p/519d	hsa-let-7c-3p	hsa-miR-4698	hsa-let-7c-3p
miR-190/190ab	hsa-let-7d-5p	hsa-miR-495-3p	hsa-let-7c-5p
miR-19ab	hsa-let-7d-5p	ebv-miR-BART22	hsa-let-7d-3p
miR-214/761/3619-5p	hsa-let-7d-5p	hsa-miR-5692a	hsa-let-7d-5p
miR-216a	hsa-let-7e-5p	hsa-miR-497-3p	hsa-let-7e-3p
miR-216b/216b-5p	hsa-let-7e-5p	hsa-miR-548ac	hsa-let-7e-5p
miR-218/218a	hsa-let-7e-3p	hsa-miR-548d-3p	hsa-let-7f-1-3p

Table S10 The relationship between target miRNAs and their corresponding lncRNAs.

miRNA	lncRNA
hsa-miR-23a-3p	AC000120.1

hsa-miR-23a-3p	NEAT1
hsa-miR-23a-3p	MALAT1
hsa-miR-23a-3p	AC007780.1
hsa-miR-23a-3p	Z93241.1
hsa-miR-23a-3p	XIST
hsa-miR-139-5p	AC093010.2
hsa-miR-139-5p	AC084082.1
hsa-miR-212-5p	MIR29B2CHG
hsa-miR-212-5p	H19
hsa-miR-212-5p	KCNQ1OT1
hsa-miR-212-5p	MALAT1
hsa-miR-212-5p	AC006064.5
hsa-miR-212-5p	AC016876.2
hsa-miR-212-5p	SNHG16
hsa-miR-380-3p	FGD5-AS1
hsa-miR-380-3p	OIP5-AS1
hsa-miR-380-3p	XIST
hsa-miR-433-3p	GAS5
hsa-miR-433-3p	NEAT1
hsa-miR-433-3p	AC125257.1
hsa-miR-433-3p	NORAD
hsa-miR-485-3p	LINC00461
hsa-miR-485-3p	NEAT1
hsa-miR-485-3p	MALAT1
hsa-miR-485-3p	SNHG14

hsa-miR-485-3p	PWAR5
hsa-miR-485-3p	ARHGAP27P1-BPTFP1-KPNA2P3
hsa-miR-485-3p	SNHG20
hsa-miR-485-3p	NORAD
hsa-miR-495-3p	AC005538.2
hsa-miR-495-3p	NEAT1
hsa-miR-495-3p	NORAD
hsa-miR-524-5p	MIR29B2CHG
hsa-miR-524-5p	FGD5-AS1
hsa-miR-524-5p	LINC-PINT
hsa-miR-524-5p	NEAT1
hsa-miR-524-5p	NORAD
hsa-miR-524-5p	XIST
hsa-miR-520g-3p	AL356488.2
hsa-miR-520g-3p	ADAMTSL4-AS1
hsa-miR-520g-3p	NEAT1
hsa-miR-520g-3p	AC023509.1
hsa-miR-520g-3p	OIP5-AS1
hsa-miR-520g-3p	AC005261.1
hsa-miR-520g-3p	NORAD
hsa-miR-520g-3p	XIST
hsa-miR-520h	AL356488.2
hsa-miR-520h	ADAMTSL4-AS1
hsa-miR-520h	NEAT1
hsa-miR-520h	AC023509.1

hsa-miR-520h	OIP5-AS1
hsa-miR-520h	AC005261.1
hsa-miR-520h	NORAD
hsa-miR-520h	XIST
hsa-miR-758-3p	AC103702.1
hsa-miR-758-3p	XIST
hsa-miR-1179	AL357507.1
hsa-miR-1179	NEAT1
hsa-miR-1179	MALAT1
hsa-miR-1179	OIP5-AS1
hsa-miR-23c	AC000120.1
hsa-miR-23c	NEAT1
hsa-miR-23c	MALAT1
hsa-miR-23c	AC007780.1
hsa-miR-23c	Z93241.1
hsa-miR-23c	XIST
hsa-miR-7853-5p	GAS5
hsa-miR-7853-5p	FGD5-AS1
hsa-miR-7853-5p	MALAT1
hsa-miR-7853-5p	XIST

Table S11 A regulatory network result of encompassing lncRNA, miRNA, and MAD2L1.

1	AC00012 0.1	hsa-miR- 23a-3p	NEAT1	hsa-miR- 23a-3p	MALAT1	hsa-miR- 23a-3p	AC00778 0.1	hsa-miR- 23a-3p	Z93241.1	hsa-miR- 23a-3p	XIST	hsa-miR- 23a-3p	AC09301 0.2
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2	hsa-miR-23a-3p	MAD2L1	hsa-miR-23a-3p	MAD2L1	hsa-miR-23a-3p	MAD2L1	hsa-miR-23a-3p	MAD2L1	hsa-miR-23a-3p	MAD2L1	hsa-miR-23a-3p	MAD2L1	hsa-miR-139-5p
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Table S12 A correlation between the mRNA expression levels of MAD family members (MAD1L1, MAD2L1, MAD2L2) and drug sensitivity by the CTPR dataset.

symbol	drug	cor	fd	entrez
MAD2L2	16-beta-bromoandrosterone	-0.125256403	0.006026553	10459
MAD2L2	1S,3R-RSL-3	-0.169737874	0.000010767	10459
MAD2L2	3-Cl-AHPC	-0.203665971	5.20489E-08	10459
MAD2L2	968	-0.080121681	0.973488613	10459
MAD2L2	A-804598	0.008341006	0.971470702	10459
MAD2L2	AA-COCF3	-0.125779891	0.002055423	10459
MAD2L2	ABT-199	-0.150499158	0.004426844	10459
MAD2L2	ABT-737	-0.134827704	0.001431528	10459
MAD2L2	AC55649	-0.018096347	0.910357769	10459
MAD2L2	AGK-2	-0.027398121	0.948276781	10459

Table S13 87 drugs identified through the CTRP in FDA-approved MAD2L1-related anti-tumor drugs.

symbol	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1	MAD2L1
drug	vincristine	cytarabine hydrochloride	clofarabine	etoposide	ciclopirox	topotecan	MK-1775	paclitaxel	gemcitabine	mitomycin	doxorubicin

Table S14 A correlation between the mRNA expression levels of MAD family members (MAD1L1, MAD2L1, MAD2L2) and drug sensitivity by the GDSC dataset.

symbol	drug	cor	fdr	entrez
MAD1L1	(5Z)-7-Oxozeaenol	-0.231851862	5.88616E-11	8379
MAD1L1	17-AAG	-0.012841643	0.759018935	8379
MAD1L1	5-Fluorouracil	-0.105879915	0.003272326	8379
MAD1L1	681640	-0.033359131	0.600557602	8379
MAD1L1	A-443654	0.052770556	0.76161772	8379
MAD1L1	A-770041	-0.025717697	0.789846437	8379
MAD1L1	AC220	-0.082269902	0.055556604	8379
MAD1L1	AG-014699	-0.001277504	0.98241697	8379
MAD1L1	AICAR	-0.079162002	0.044760325	8379
MAD1L1	AKT inhibitor VIII	0.146857099	0.000300332	8379

Table S15 25 drugs identified through the GDSC in FDA-approved MAD2L1-related anti-tumor drugs.

symbol	drug	cor	fdr	entrez
MAD2L1	Trametinib	0.276120643	0	4085
MAD2L1	selumetinib	0.242901964	8.55534E-13	4085
MAD2L1	Navitoclax	-0.240847457	9.55921E-12	4085
MAD2L1	Vorinostat	-0.240200898	1.00012E-11	4085
MAD2L1	Bleomycin (50 uM)	0.183448841	1.45359E-07	4085
MAD2L1	Gefitinib	0.187202936	6.49013E-07	4085
MAD2L1	AZD7762	-0.18433452	7.60264E-07	4085
MAD2L1	Methotrexate	-0.175655411	9.64336E-07	4085

MAD2L1	Afatinib	0.166323254	1.83461E-06	4085
MAD2L1	Belinostat	-0.155078199	0.000014789	4085
MAD2L1	Docetaxel	0.147026945	0.000061176	4085
MAD2L1	PAC-1	-0.143461056	0.000199664	4085
MAD2L1	Lapatinib	0.204066745	0.000443622	4085
MAD2L1	Masitinib	-0.125439807	0.00052662	4085
MAD2L1	Cetuximab	0.126232893	0.0009748	4085
MAD2L1	Erlotinib	0.196861768	0.002201115	4085
MAD2L1	AICAR	-0.116096013	0.00245187	4085
MAD2L1	Phenformin	-0.099877285	0.00631339	4085
MAD2L1	5-Fluorouracil	-0.092236942	0.010955917	4085
MAD2L1	CEP-701	-0.096596754	0.013774022	4085
MAD2L1	Dabrafenib	0.097001614	0.015583776	4085
MAD2L1	Nilotinib	-0.099693484	0.025598723	4085
MAD2L1	Camptothecin	-0.091208067	0.026709251	4085
MAD2L1	Bryostatin 1	0.095061037	0.039577197	4085
MAD2L1	Dasatinib	0.127200454	0.04409342	4085

Table S16 The TCGA database was used to identify genes that were co-expressed.

id	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	gene_name	gene_type
ENSG00000000003.15	5158.243771	0.133281769	0.083106543	1.603745785	0.108770099	0.166845846	TSPAN6	protein_coding
ENSG00000000005.6	41.66468037	-0.183113475	0.175604528	-1.042760555	0.297059204	0.383478692	TNMD	protein_coding
ENSG000000000419.13	1755.820795	0.376741021	0.063421692	5.940254954	2.84579E-09	2.82645E-08	DPM1	protein_coding
ENSG000000000457.14	443.6306	0.028474633	0.039490666	0.721047169	0.470880494	0.555405766	SCYL3	protein_coding

ENSG00000000460.17	334.4971426	0.349001157	0.050725567	6.880182432	5.9776E-12	1.06399E-10	C1orf112	protein_coding
ENSG00000000938.13	255.1366622	-0.443530266	0.110569211	-4.01133609	6.03761E-05	0.000228651	FGR	protein_coding
ENSG00000000971.16	764.2589488	-0.398273134	0.107187366	-3.715672384	0.000202664	0.000675991	CFH	protein_coding
ENSG00000001036.14	2242.10878	0.14234882	0.044073289	3.229820682	0.001238679	0.003376969	FUCA2	protein_coding
ENSG00000001084.13	1472.776452	0.114762949	0.042461077	2.702779995	0.006876224	0.015336834	GCLC	protein_coding
ENSG00000001167.14	1096.770099	0.076977261	0.038413276	2.003923359	0.045078271	0.079006553	NFYA	protein_coding

Table S17 The top 500 co-expressed genes using GO and KEGG to identify biological processes, cellular components, and molecular functions.

ID	Description	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
GO:0007059	chromosome segregation	47/439	348/18800	1.35936E-22	4.7795E-19	4.42864E-19	MAD2L1/ESCO2/NCAPG/NUF2/CENPK/DLGAP5/	47
GO:0000280	nuclear division	52/439	446/18800	6.2957E-22	1.10678E-18	1.02554E-18	MAD2L1/EGF/EREG/DMRT1/NCAPG/RAD51AP1/NUF2	52
GO:0000779	condensed chromosome, centromeric region	32/465	156/19594	4.49045E-21	1.25E-18	1.1216E-18	MAD2L1/CENPU/NCAPG/NUF2/CENPK/CCNB1/CENPE	32
GO:0000776	kinetochore	31/465	146/19594	6.3613E-21	1.25E-18	1.1216E-18	MAD2L1/CENPU/NUF2/CENPK/CCNB1/CENPE/BIRC5	31
GO:0098687	chromosomal region	45/465	366/19594	1.07063E-19	9.88634E-18	8.87083E-18	MAD2L1/ESCO2/CENPU/CDK1/NCAPG/RAD51AP1/NUF2	45

Table S18 WB validation protein concentration determination data.

Standard reference number	1	2	3	4	5	6	7	8
Standard OD	0.1598	0.3886	0.6001	0.797	0.9396	1.3079	1.6153	1.8776
Standard samples OD	0	0.2288	0.4403	0.6372	0.7798	1.1481	1.4555	1.7178

Standard concentration ($\mu\text{g}/\mu\text{L}$)	0	0.1	0.2	0.3	0.4	0.6	0.8	1.0
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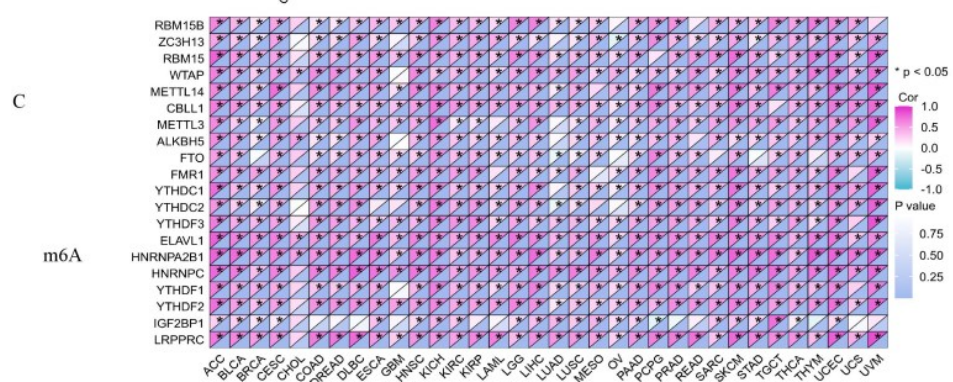
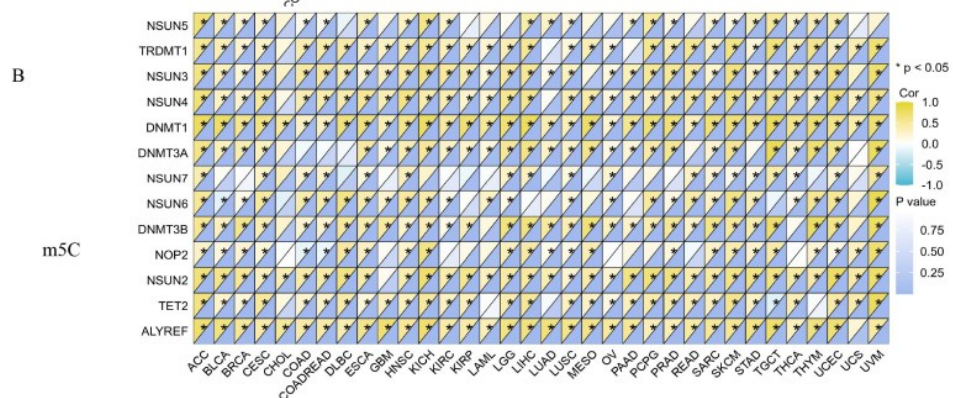
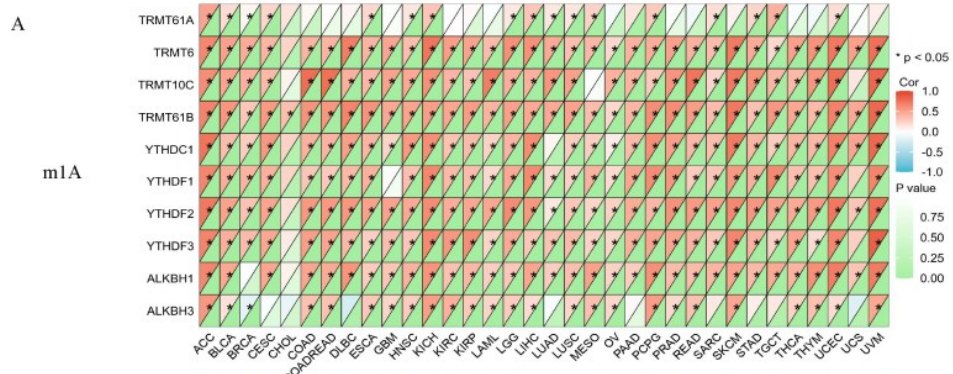
Table S19 Cell cycle assay data

Number	Specimen	Sample	Freq G1	Freq S	Freq G2
6	HCT116 cell cycle	NC(1)	42.81	46.99	9.59
6	HCT116 cell cycle	NC(2)	38.61	45.35	15.61
6	HCT116 cell cycle	NC(3)	38.86	46.12	14.36
6	HCT116 cell cycle	MAD2L1-si406(1)	43.01	38.67	17.93
6	HCT116 cell cycle	MAD2L1-si406(2)	42.62	42.28	14.43
6	HCT116 cell cycle	MAD2L1-si406(3)	40.56	40.7	18.05
7	RKO cell cycle	NC(1)	47.99	40.91	10.56
7	RKO cell cycle	NC(2)	48.83	41.9	8.5
7	RKO cell cycle	NC(3)	51.45	38.39	9.38
7	RKO cell cycle	MAD2L1-si406(1)	49.02	38.02	12.19
7	RKO cell cycle	MAD2L1-si406(2)	50.12	37.23	12.09
7	RKO cell cycle	MAD2L1-si406(3)	51.14	36.85	11.41

Table S20 Cell apoptosis detection data.

Number	Specimen	Sample	Q2-2 % Parent	Q2-4 % Parent
4	Apoptosis of HCT116 cells	NC(1)	1.11%	5.78%
4	Apoptosis of HCT116 cells	NC(2)	1.09%	6.79%
4	Apoptosis of HCT116 cells	NC(3)	1.26%	6.51%
4	Apoptosis of HCT116 cells	MAD2L1-si406(1)	0.49%	8.46%
4	Apoptosis of HCT116 cells	MAD2L1-si406(2)	0.60%	8.67%

4	Apoptosis of HCT116 cells	MAD2L1-si406(3)	0.39%	9.06%
5	Apoptosis of RKO cells	NC(1)	8.05%	9.20%
5	Apoptosis of RKO cells	NC(2)	8.98%	8.17%
5	Apoptosis of RKO cells	NC(3)	9.08%	9.12%
5	Apoptosis of RKO cells	MAD2L1-si406(1)	11.86%	10.15%
5	Apoptosis of RKO cells	MAD2L1-si406(2)	12.01%	10.63%
5	Apoptosis of RKO cells	MAD2L1-si406(3)	12.19%	10.38%



MAD2L1 Expression Levels

Fig. S2 Illustrates the correlation analysis between **MAD2L1** expression and the methylation regulatory factors involved in mRNA modification. (A) m1A, (B) m5C, and (C) m6A. The correlation is assessed based on Pearson's rho value and its statistical significance, with a threshold of (*P<0.05).

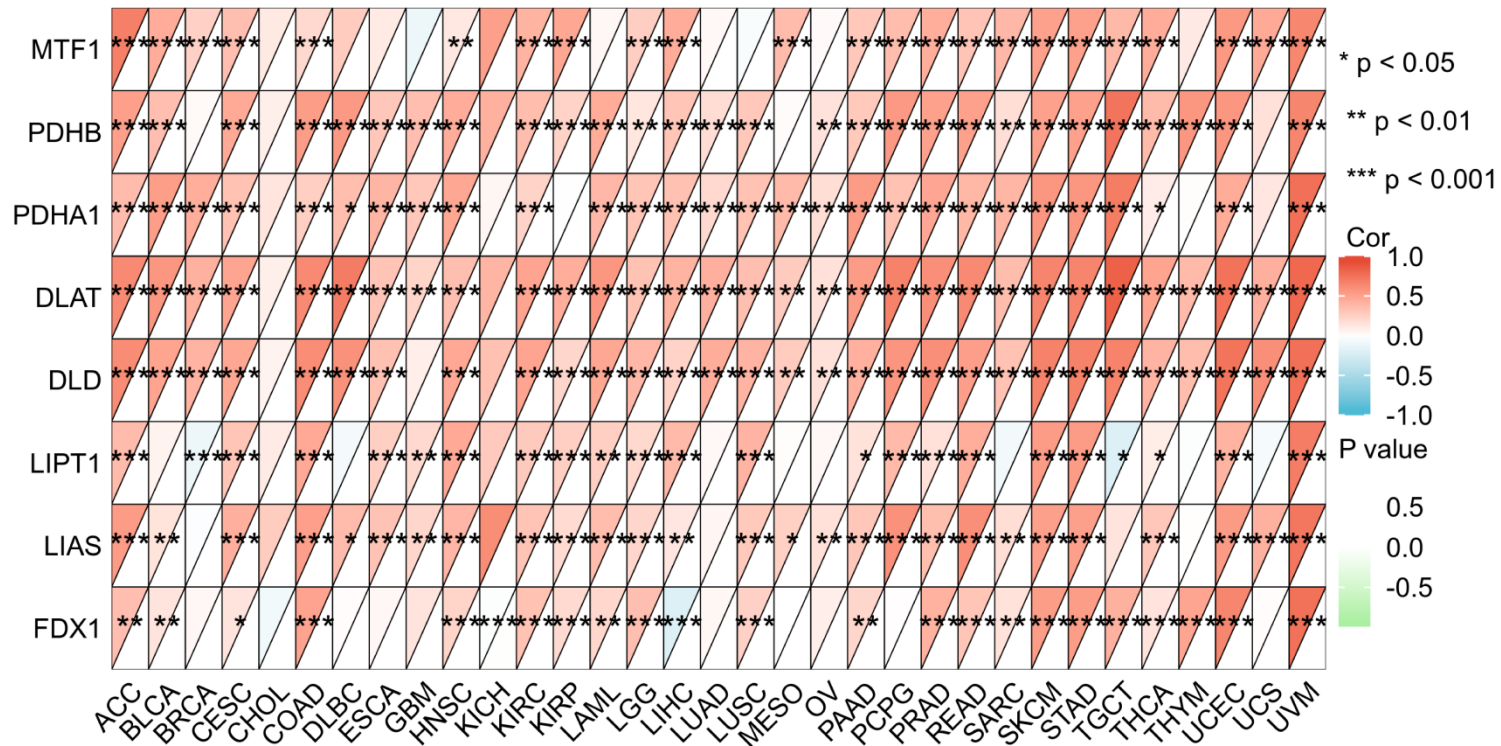


Fig. S3 Analysis of the relationship between copper apoptosis-related genes and pan-oncogene (MAD2L1) expression. (*P < 0.05, **P < 0.01, *P < 0.001)**

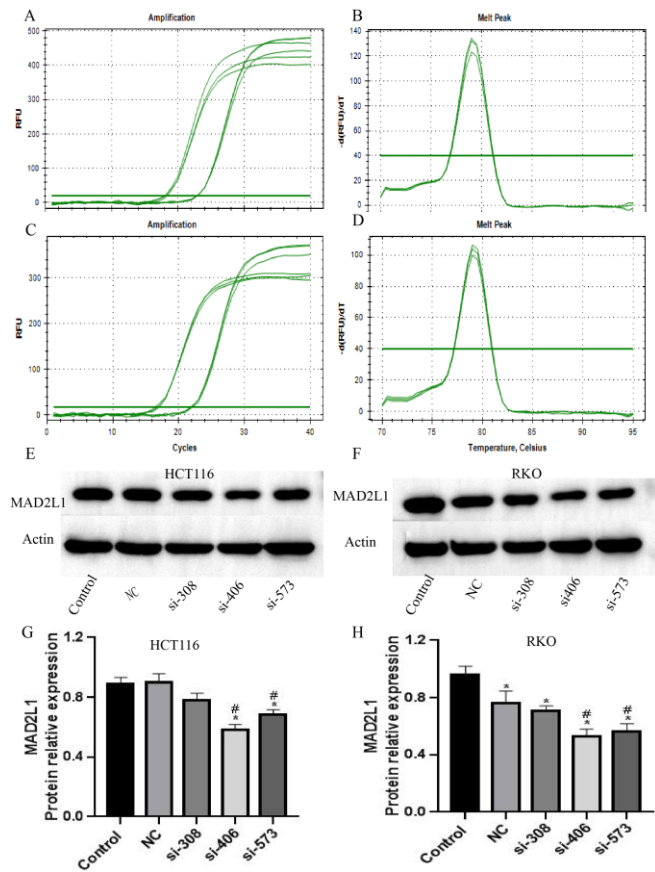


Fig. S4 Verification of interference efficiency.(A-D)Background verification of MAD2L1 in HCT116 and RKO.(E-H)Verification of interference efficiency.