Supplementary Data

Figure legends

Supplementary Fig. 1 TH1579 affects human and murine mesothelioma cell viability. ZL35, MSTO-211H human mesothelioma and AB1 and AE17 murine mesothelioma cells were seeded at $3x10^3$ cells/well in 96-well plates. The day after, cells were treated with vehicle or TH1579 (1-1000μM) and 24 h later cell viability was measured by XTT reduction. Data are presented as mean±SEM, n=6 for each group, *p<0.05 compared to vehicle by 2-tailed students' T test

Supplementary Fig. 2 Pharmacological targeting of MTH1 elevates H2AX levels in mesothelioma tumor cells. Tumor tissue sections of murine mesothelioma tumors were stained for γH2Ax (A) Representative pictures. (B) Data presented as mean±SEM, vehicle n=6, TH1579 n=4, *p<0.05 compared to vehicle by 2-tailed students' T test. HPF: High Power Field. Scale bar: 100μm

Supplementary Fig. 3 MTH1 expression is high in AB1 cells and low in AE17 and was modulated by using short hairpin RNAs targeting *Mth1* in the former or by introducing an MTH1 overexpressing vector to the latter. AB1 or AE17 murine mesothelioma cells were seeded at $5x10^4$ cells/well in 6-well plates. The day after, AB1 cells were transfected with murine *Nudt1* shRNA Plasmid, while AE17 with Mth1ORF expression plasmid and transfected clones were isolated upon G418 selection (500μ/ml) for 7 days. MTH1 expression was quantified by western blot. Representative blots of three independent experiments and results of densitometric analysis. Data presented as mean±SEM, n=3 for each group, *p<0.05 compared to AB1 by 2-tailed students' T test.

Supplementary Fig. 4 MTH1 gene expression is down regulated by NFKB activation in endothelial cells. (A) Serum starved endothelial cells were treated with

NFKB inducers TNFA (20ng/ml) (n=3) and PMA (5μM) (n=3) for 4h or vehicle (n=4) and MTH1 expression was measured 18h later. (B, C) Tumor cell cfDNA effects are mediated through NFKB. Serum starved AE17 tumor endothelial cells were treated with BAY11-7082 (10μM) (n=3), TNFA (20ng/ml) (n=3) or vehicle (n=4) for 40min and subsequently treated with 30ng cell free DNA (CfDNA) from AE17 (C) or AE17mth1 overexpressing cells (B) for 18h. Expression of MTH1 was measured by western blot. Shown are representative blots of three independent experiments. Data are presented as mean±SEM, *p<0.05 compared to vehicle by One-way ANOVA (with Bonferroni post hoc test).

Supplementary Table 1. List of differentially expressed genes between 'high' and 'low' *MTH1* expressing mesotheliomas. Between-group differential expression analysis was conducted using the edgeR package in R, after TMM normalization of raw counts was performed. The glmTreat function of edgeR was implemented for testing significant differences relative to fold-change thresholds. Genes with an adjusted p-value (Benjamini–Hochberg multiple hypothesis testing correction for False Discovery Rate control) < 0.05 and |log2(Fold Change)|> 0.3 were considered as differentially expressed.

Supplementary Table 2. List of significantly associated GO terms of biological processes derived by enrichment analysis of DEGs between 'high' and 'low' *MTH1* expressing mesotheliomas.

Supplementary Table 3. List of significantly associated GO terms of cellular components derived by enrichment analysis of DEGs between 'high' and 'low' *MTH1* expressing mesotheliomas.
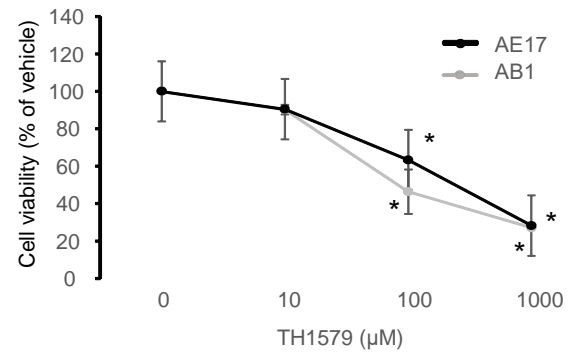
Supplementary Table 4. List of significantly associated Reactome Pathway terms derived by enrichment analysis of DEGs between 'high' and 'low' *MTH1* expressing mesotheliomas.

Supplementary Fig. 1

A
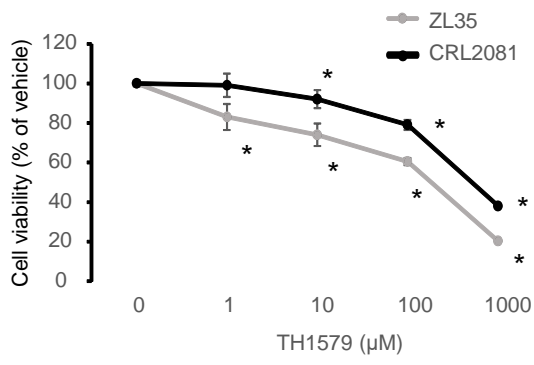
B

Supplementary Fig. 2

TH1579 AB1
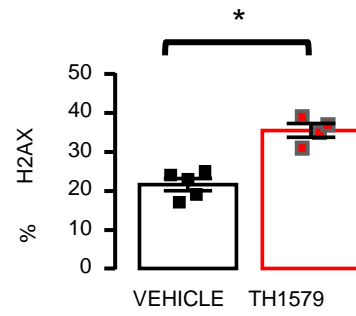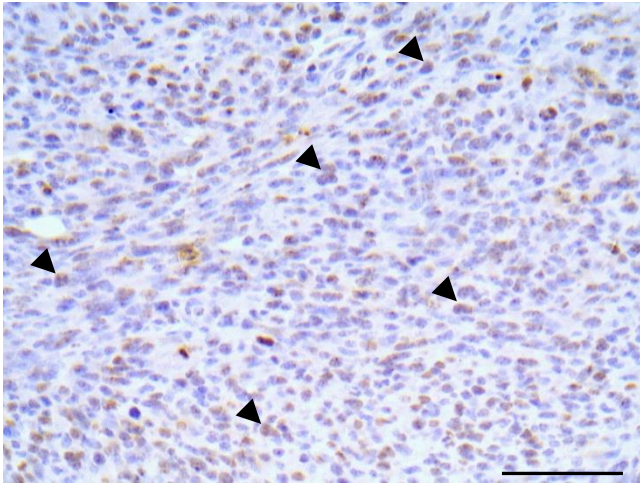
VEHICLE AB1
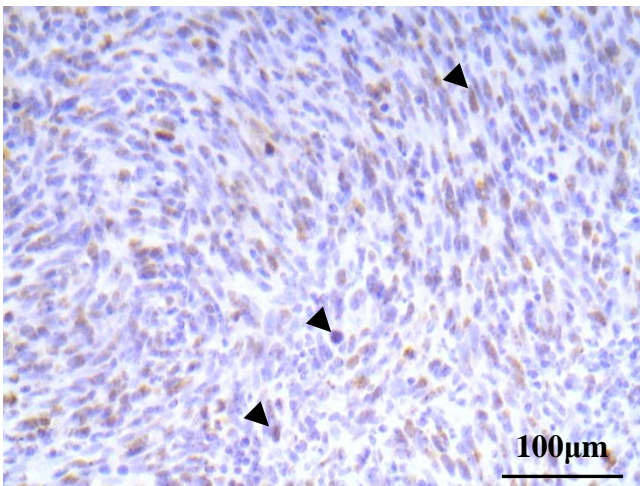
Arrowheads depicts positive nuclear staining; scale bar 100μm

Supplementary Fig. 3
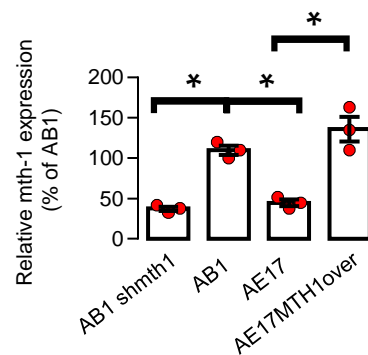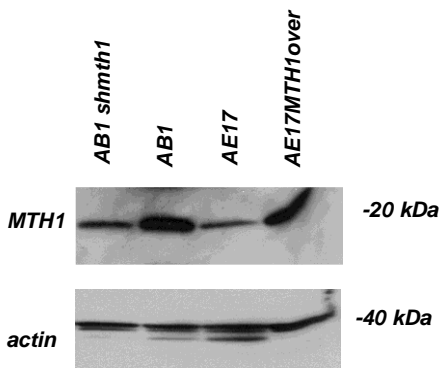
Supplementary Fig. 4

A

MTH1

actin

Ctl   TNF-α   PMA

18h

Relative MTH1 expression

*

0.4
0.3
0.2
0.1
0.0

B

Cf AE17mth1over
Cf AE17mth1over+ BAY11-7082
Cf AE17mth1over+ TNF-α

MTH1

actin

18h

Relative MTH-1 expression

*

0.6
0.4
0.2
0.0

C

Cf AE17
Cf AE17+ BAY11-7082
Cf AE17+ TNF-α

MTH1

actin

18h

Relative MTH1 expression

*
*

0.8
0.6
0.4
0.2
0.0

Supplementary Table 1
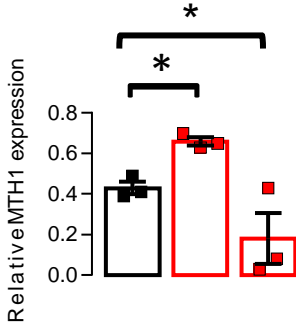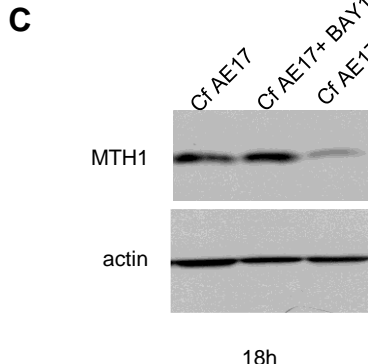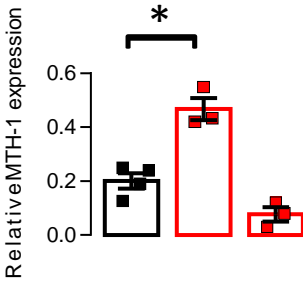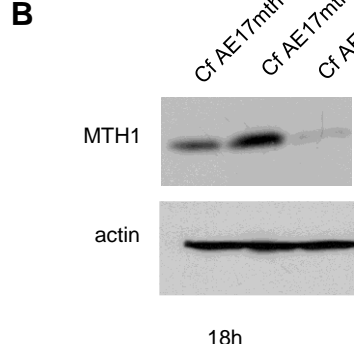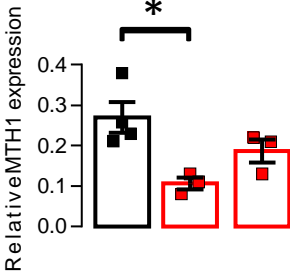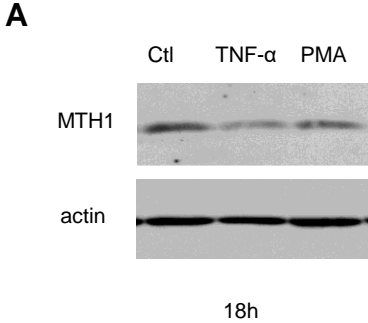
Gene Symbol	HGNC approved Gene Symbol	ENTREZ ID	logFC	logCPM	PValue	FDR (adjusted Pvalue)
NUDT1	NUDT1	4521	1,637203032	4,248514099	3,38059E-10	4,76055E-06
KIAA1244	ARFGEF3	57221	-2,671426344	3,766499252	2,6199E-06	0,006626884
NBEAL1	NBEAL1	65065	-1,962630743	1,790482285	2,21247E-06	0,006626884
WWC2	WWC2	80014	-1,529119318	5,875021094	9,71096E-07	0,006626884
WDFY3	WDFY3	23001	-1,109675798	5,170533781	3,29415E-06	0,006626884
ANKRD17	ANKRD17	26057	-1,108660121	6,092621774	2,94127E-06	0,006626884
CENPM	CENPM	79019	1,660753313	2,406441248	2,29192E-06	0,006626884
FAM63B	MINDY2	54629	-2,076590094	4,065084689	3,97431E-06	0,006995775
TOR1AIP2	TOR1AIP2	163590	-1,497155778	4,824989495	7,56198E-06	0,010648775
ZNF428	ZNF428	126299	1,083823026	5,538959375	7,42525E-06	0,010648775
FAM160A1	FAM160A1	729830	-2,13298301	1,873164395	1,05072E-05	0,013451127
CLOCK	CLOCK	9575	-1,590166149	3,740724095	1,15711E-05	0,013578734
AFF1	AFF1	4299	-1,215211573	6,615922367	1,41333E-05	0,015309629
ABO	ABO	28	-2,356683743	0,490964988	1,67767E-05	0,016875005
KLHL11	KLHL11	55175	-1,82516978	0,519702593	2,25542E-05	0,017644886
UTP14C	UTP14C	9724	-0,938481576	5,194384505	2,00944E-05	0,017644886
MPG	MPG	4350	1,064098698	6,440276178	2,19655E-05	0,017644886
EMID2	COL26A1	136227	5,267355917	4,303610128	2,08325E-05	0,017644886
MAP3K2	MAP3K2	10746	-1,103321084	4,638849457	2,5438E-05	0,018853591
SGMS2	SGMS2	166929	-2,478413548	6,250451125	3,66662E-05	0,02023009
PARD3B	PARD3B	117583	-2,021998782	2,55228635	3,73514E-05	0,02023009
SLC30A1	SLC30A1	7779	-1,346815119	4,044839653	3,61263E-05	0,02023009
ATP2B4	ATP2B4	493	-1,106738729	7,995111062	3,06176E-05	0,02023009
SEC24B	SEC24B	10427	-0,902221173	5,330001085	3,65876E-05	0,02023009
WASH5P	WASH5P	375690	1,21066703	3,586047651	2,99406E-05	0,02023009
MXD3	MXD3	83463	1,221336682	4,177826734	3,49453E-05	0,02023009
MRPL28	MRPL28	10573	1,075135257	6,314501838	4,2499E-05	0,022165588
SMARCAD1	SMARCAD1	56916	-0,943958071	4,792321072	4,93495E-05	0,02481928
TAOK1	TAOK1	57551	-1,911033402	3,387060818	7,15852E-05	0,026573339
SOCS7	SOCS7	30837	-1,861288911	1,208090686	7,64299E-05	0,026573339
DKFZp686O24166	NCR3LG1	374383	-1,661662246	2,245491655	6,56103E-05	0,026573339
ZKSCAN1	ZKSCAN1	7586	-1,499252396	4,644443032	7,15896E-05	0,026573339
ASH1L	ASH1L	55870	-1,127902593	6,068899056	6,63845E-05	0,026573339
SDAD1	SDAD1	55153	-0,888468751	5,060993366	7,28126E-05	0,026573339
MLST8	MLST8	64223	0,83092888	5,653905803	7,45556E-05	0,026573339
ASPSCR1	ASPSCR1	79058	0,874885701	4,884600852	5,88299E-05	0,026573339
WRAP53	WRAP53	55135	0,983078612	3,801989686	6,63177E-05	0,026573339
AP2S1	AP2S1	1175	1,021113191	6,721073094	7,73688E-05	0,026573339
NMRAL1	NMRAL1	57407	1,040389123	5,741496727	5,52319E-05	0,026573339
JOSD2	JOSD2	126119	1,247862018	5,163613012	6,34981E-05	0,026573339
KCNN4	KCNN4	3783	2,78377451	5,220976766	6,65816E-05	0,026573339
FAM73A	MIGA1	374986	-1,09440762	3,761020032	8,65248E-05	0,028335864
GADD45GIP1	GADD45GIP1	90480	1,246543193	6,223295395	8,4981E-05	0,028335864
NEB	NEB	4703	-5,259755487	4,412720057	9,36526E-05	0,0299731
LDB3	LDB3	11155	-3,628527969	2,397188576	0,00010115	0,031322014
CEP350	CEP350	9857	-0,868931221	5,514201083	0,000102848	0,031322014
PEX16	PEX16	9409	0,806702492	4,872086155	0,00010454	0,031322014
GCC2	GCC2	9648	-0,935606169	5,307224507	0,000108671	0,031881275
C16orf13	METTL26	84326	1,254764541	5,988927274	0,000111618	0,032077555
RAB3GAP2	RAB3GAP2	25782	-0,818342697	5,381454094	0,000114478	0,032241501
TACSTD2	TACSTD2	4070	-4,891789541	5,110280687	0,000130954	0,034060117
UHMK1	UHMK1	127933	-2,084654492	3,688409973	0,000157817	0,034060117
HIPK3	HIPK3	10114	-1,786771062	5,228120529	0,000175228	0,034060117
HERC3	HERC3	8916	-1,713446839	4,742855039	0,000160622	0,034060117
ZNF641	ZNF641	121274	-1,510623875	3,81037359	0,000192915	0,034060117
ROCK2	ROCK2	9475	-1,489780195	5,216333618	0,000169337	0,034060117
MCTP2	MCTP2	55784	-1,418352158	5,054399854	0,000188579	0,034060117
RNF169	RNF169	254225	-1,304958288	4,723159127	0,00013331	0,03406011
CD46	CD46	4179	-1,083769941	7,831772685	0,000164461	0,034060117

Supplementary Table 1 cont

Gene Symbol	HGNC approved Gene Symbol	ENTREZ ID	logFC	logCPM	PValue	FDR (adjusted Pvalue)
RAPGEF2	RAPGEF2	9693	-1,070311901	5,032218816	0,00019408	0,034060117
RBBP5	RBBP5	5929	-1,057356645	4,094383372	0,000154728	0,034060117
KIAA1109	KIAA1109	84162	-1,057259991	5,584570462	0,000200752	0,034060117
OTUD7B	OTUD7B	56957	-0,927750985	5,207236176	0,000190997	0,034060117
DIS3	DIS3	22894	-0,841617097	5,311774593	0,000158329	0,034060117
MED13	MED13	9969	-0,832652889	6,174393578	0,000142109	0,034060117
ATF6	ATF6	22926	-0,82528914	5,897609134	0,000167975	0,034060117
RAB33B	RAB33B	83452	-0,809559625	3,354801085	0,000193528	0,034060117
CDC73	CDC73	79577	-0,751090217	5,210083622	0,000144411	0,034060117
DRAP1	DRAP1	10589	0,848857477	6,617276302	0,000186962	0,034060117
PSMG3	PSMG3	84262	0,854198722	5,231922579	0,000176961	0,034060117
FASTK	FASTK	10922	0,898957679	6,556629536	0,00017738	0,034060117
NDUFS6	NDUFS6	4726	1,00198944	6,435285469	0,000128849	0,034060117
BCL7C	BCL7C	9274	1,010944692	5,373067167	0,000131851	0,034060117
C6orf226	C6orf226	441150	1,104246779	2,372043601	0,000195719	0,034060117
CHTF18	CHTF18	63922	1,10690264	4,413970251	0,000195427	0,034060117
POC1A	POC1A	25886	1,112760911	3,061857891	0,000143064	0,034060117
TACC3	TACC3	10460	1,171093009	5,736429537	0,000179086	0,034060117
PTTG1	PTTG1	9232	1,294227929	4,322957973	0,000171545	0,034060117
ATP5D	ATP5F1D	513	1,36364488	6,367123739	0,000198676	0,034060117
DNLZ	DNLZ	728489	1,518428451	3,449556211	0,000153785	0,034060117
APOE	APOE	348	1,593756608	8,68459978	0,000148604	0,034060117
PIF1	PIF1	80119	1,726031655	2,113288234	0,000151264	0,034060117
SYCE1L	SYCE1L	100130958	2,118286578	1,040507645	0,000200544	0,034060117
PIK3CA	PIK3CA	5290	-1,06833405	4,15597371	0,000216694	0,034709557
OTUD4	OTUD4	54726	-1,066197008	5,644293	0,000214625	0,034709557
COMMD1	COMMD1	150684	0,943442539	4,318459739	0,000215562	0,034709557
NOSIP	NOSIP	51070	0,958876767	5,645488841	0,000216904	0,034709557
C4orf48	C4orf48	401115	1,940430196	3,727969607	0,000207452	0,034709557
SLC4A4	SLC4A4	8671	-2,123694309	5,928459946	0,000222591	0,034828139
FBXO28	FBXO28	23219	-0,696929133	5,247608143	0,000220483	0,034828139
C1orf55	SDE2	163859	-1,033814043	4,508341843	0,000225586	0,034908857
OSMR	OSMR	9180	-1,45771358	6,917498054	0,000233308	0,034999198
CPNE3	CPNE3	8895	-0,850530232	6,740653195	0,000233626	0,034999198
DTYMK	DTYMK	1841	1,095062013	4,908439584	0,000230767	0,034999198
PTPN14	PTPN14	5784	-1,435240854	4,175252864	0,000265632	0,03622604
ARHGEF35	ARHGEF35	445328	-1,359156609	4,567913194	0,000266557	0,03622604
ARHGEF12	ARHGEF12	23365	-1,199451474	7,263707262	0,000252587	0,03622604
MLXIP	MLXIP	22877	-1,087232902	5,696668765	0,000270113	0,03622604
MTR	MTR	4548	-0,906324873	5,752291877	0,00026006	0,03622604
TPR	TPR	7175	-0,86644207	7,497748621	0,000268892	0,03622604
BANF1	BANF1	8815	0,78699859	7,245540228	0,000257171	0,03622604
REEP4	REEP4	80346	0,863631715	5,007312792	0,000254821	0,03622604
APRT	APRT	353	0,882273382	6,901689971	0,000261335	0,03622604
HINT2	HINT2	84681	1,214618011	4,762009426	0,000269409	0,03622604
RECQL4	RECQL4	9401	1,423890029	4,092881551	0,000255932	0,03622604
FBXL3	FBXL3	26224	-0,908339946	5,300374898	0,000282945	0,037588933
MCM5	MCM5	4174	0,877354631	5,632050277	0,000287268	0,037806599
ATP2A1	ATP2A1	487	-4,273918664	3,703748639	0,000330143	0,038460045
KLF5	KLF5	688	-1,259212784	5,57167579	0,000327603	0,038460045
LARP1B	LARP1B	55132	-1,230832238	3,766877414	0,000312127	0,038460045
AKAP9	AKAP9	10142	-0,983877128	5,900805227	0,000314003	0,038460045
USP38	USP38	84640	-0,885324557	4,786030088	0,000318868	0,038460045
EXOC8	EXOC8	149371	-0,820930938	4,455517618	0,000327884	0,038460045
G3BP2	G3BP2	9908	-0,766358503	6,717628263	0,00030666	0,038460045
POLD1	POLD1	5424	0,812872241	5,249854501	0,000319361	0,038460045
SNRPD2	SNRPD2	6633	0,856333751	7,535102055	0,000306761	0,038460045
NDUFB10	NDUFB10	4716	0,898235514	6,455154603	0,000328563	0,038460045
TRAPPC1	TRAPPC1	58485	0,913172245	6,636973942	0,000303207	0,038460045
PGP	PGP	283871	0,983538045	4,504841378	0,000330469	0,038460045

Gene Symbol	HGNC approved Gene Symbol	ENTREZ ID	logFC	logCPM	PValue	FDR (adjusted Pvalue)
CEMP1	CEMP1	752014	1,553078181	4,220632894	0,000304186	0,038460045
RHBDL1	RHBDL1	9028	1,738235994	1,515032906	0,000311282	0,038460045
USO1	USO1	8615	-0,914857495	6,476279535	0,000334439	0,038603073
KCND3	KCND3	3752	-2,383339423	1,488221363	0,000339898	0,038673435
RIF1	RIF1	55183	-1,171874632	4,627682653	0,000340542	0,038673435
MBNL2	MBNL2	10150	-0,925918817	6,030518088	0,000348579	0,038957903
ZFPM1	ZFPM1	161882	1,088356303	3,380309206	0,00034799	0,038957903
SYNE2	SYNE2	23224	-1,735887067	6,456946152	0,000361249	0,0390962
NAF1	NAF1	92345	-1,062196205	3,036993568	0,00036711	0,0390962
SNRPA	SNRPA	6626	0,725086498	6,09659099	0,000366014	0,0390962
FAM86A	EEF2KMT	196483	0,860420222	4,333023418	0,000364301	0,0390962
RABAC1	RABAC1	10567	0,956260298	6,83153469	0,000359532	0,0390962
C17orf90	OXLD1	339229	0,97826259	4,697472335	0,000369251	0,0390962
ATOX1	ATOX1	475	1,117811468	5,678164869	0,000357602	0,0390962
SHISA3	SHISA3	152573	-3,371336233	2,40575809	0,000375935	0,039506828
AGER	AGER	177	-4,552770557	6,307981294	0,000451592	0,040292348
CA3	CA3	761	-3,931962578	4,126453291	0,000429433	0,040292348
S100A1	S100A1	6271	-3,716528992	3,805217477	0,00043025	0,040292348
LRRC55	LRRC55	219527	-2,563906979	0,908967272	0,000458013	0,040292348
GCNT4	GCNT4	51301	-1,903915568	0,648591009	0,000451853	0,040292348
CCNT1	CCNT1	904	-1,825565988	2,082117049	0,000400235	0,040292348
ADAMTS15	ADAMTS15	170689	-1,763705676	5,038586213	0,000458817	0,040292348
LMTK2	LMTK2	22853	-1,503657166	3,706354323	0,000448539	0,040292348
PAFAH1B2	PAFAH1B2	5049	-1,164999818	4,286897489	0,000402799	0,040292348
GTF3C4	GTF3C4	9329	-1,057628733	3,793390564	0,00044547	0,040292348
PDLIM5	PDLIM5	10611	-1,016008886	7,162373094	0,000463521	0,040292348
KIDINS220	KIDINS220	57498	-0,908925997	6,507671456	0,000451411	0,040292348
INTS6	INTS6	26512	-0,888740271	4,431028301	0,000407548	0,040292348
EDEM3	EDEM3	80267	-0,858314838	5,573296731	0,000461265	0,040292348
AKAP11	AKAP11	11215	-0,846220471	5,21550263	0,00042395	0,040292348
SMEK2	PPP4R3B	57223	-0,773594371	6,197706448	0,00043824	0,040292348
SHFM1	SEM1	7979	0,740580118	6,909759281	0,000456758	0,040292348
NARFL	CIAO3	64428	0,780098421	5,093848474	0,000405687	0,040292348
PSMC3	PSMC3	5702	0,808602177	7,445508717	0,000431715	0,040292348
ZNHIT1	ZNHIT1	10467	0,840024407	6,541043526	0,000425945	0,040292348
MRPS34	MRPS34	65993	0,843532046	6,223967184	0,000427418	0,040292348
MTG1	MTG1	92170	0,845045531	4,85160551	0,000444088	0,040292348
FAM173A	FAM173A	65990	1,044897875	3,402509969	0,000396392	0,040292348
MGC70857	C8orf82	414919	1,058905831	4,689421369	0,000463525	0,040292348
UBE2S	UBE2S	27338	1,063726136	4,646621863	0,000442932	0,040292348
SAC3D1	SAC3D1	29901	1,215361043	3,964016178	0,000395952	0,040292348
MRPL41	MRPL41	64975	1,359746573	5,4819003	0,000443082	0,040292348
VGF	VGF	7425	3,464110807	2,106704653	0,000461737	0,040292348
CRIM1	CRIM1	51232	-1,440808169	8,845095774	0,000472087	0,040784841
ERN1	ERN1	2081	-1,677731093	3,460330066	0,000479715	0,040920081
TMSB10	TMSB10	9168	0,938371859	10,7550631	0,000479406	0,040920081
NDUFB7	NDUFB7	4713	0,981425743	6,714953125	0,00048237	0,040920081
ETV3	ETV3	2117	-1,4923578	2,445622587	0,000488095	0,041043014
KIF22	KIF22	3835	0,859458613	5,799033799	0,000489648	0,041043014
PCDHGB1	PCDHGB1	56104	-3,155984125	2,647364526	0,000510029	0,041101115
ZC3HAV1L	ZC3HAV1L	92092	-1,643830089	1,271091007	0,000506361	0,041101115
MED1	MED1	5469	-0,675028534	5,747737348	0,000516302	0,041101115
NDUFS3	NDUFS3	4722	0,744415722	6,309766648	0,00051661	0,041101115
FLYWCH2	FLYWCH2	114984	0,818365587	4,513664732	0,000513789	0,041101115
CDK5	CDK5	1020	0,883311177	4,417314584	0,000508202	0,041101115
NAGLU	NAGLU	4669	0,893567737	5,920250902	0,000497137	0,041101115
CENPH	CENPH	64946	0,934512628	2,98939642	0,000511115	0,041101115
CDT1	CDT1	81620	1,411934307	4,210379133	0,000499868	0,041101115
CENPP	CENPP	401541	1,139593125	2,510928166	0,0005199	0,041130516
C1orf58	BROX	148362	-1,31689863	3,509917404	0,00052343	0,041178454

Supplementary Table 1 cont

Gene Symbol	HGNC approved Gene Symbol	ENTREZ ID	logFC	logCPM	PValue	FDR (adjusted Pvalue)
PSMB3	PSMB3	5691	0,854347119	7,071839172	0,000528722	0,041363646
DNAJB14	DNAJB14	79982	-0,959124754	3,138196609	0,000544664	0,042375493
IDH2	IDH2	3418	0,934216569	6,078802428	0,000555431	0,042975705
NTHL1	NTHL1	4913	0,969276732	3,339647633	0,000558838	0,04300302
MRPL51	MRPL51	51258	0,755273351	6,667577862	0,000563362	0,043115591
PDZD8	PDZD8	118987	-1,399854378	4,086420993	0,000567154	0,043171142
AQP3	AQP3	360	-4,035802905	6,280685053	0,000585683	0,043429397
KDR	KDR	3791	-1,755659041	7,856053128	0,000591507	0,043429397
SECISBP2L	SECISBP2L	9728	-1,062188968	5,580526007	0,000589956	0,043429397
LRBA	LRBA	987	-0,93924805	5,384795429	0,000579773	0,043429397
TWF2	TWF2	11344	0,833457962	6,50214079	0,000593793	0,043429397
ZMAT5	ZMAT5	55954	0,844192548	3,615860803	0,000595219	0,043429397
NUDT18	NUDT18	79873	1,029187995	3,959484005	0,000593083	0,043429397
C6orf26	SAPCD1	401251	1,128226196	1,082289012	0,000578325	0,043429397
BMPR2	BMPR2	659	-0,935687376	6,780534178	0,000605437	0,043947222
ZNF770	ZNF770	54989	-0,863486257	5,118865099	0,000629916	0,043989757
FNDC3A	FNDC3A	22862	-0,828842306	6,152683823	0,00062647	0,043989757
BTBD7	BTBD7	55727	-0,808714778	4,557981384	0,000613647	0,043989757
SEC31A	SEC31A	22872	-0,648516897	7,725659208	0,000610128	0,043989757
THOC6	THOC6	79228	0,844549671	5,572278775	0,000617152	0,043989757
LSM7	LSM7	51690	0,906727732	5,380119111	0,000624839	0,043989757
LRDD	PIDD1	55367	1,132492882	4,640775312	0,000631013	0,043989757
C9orf100	ARHGEF39	84904	1,25478528	2,618186968	0,00063	0,043989757
GSTZ1	GSTZ1	2954	1,051241922	3,667006014	0,000644366	0,044120775
LSMD1	NAA38	84316	1,051626139	5,337108454	0,000648936	0,044120775
ETFB	ETFB	2109	1,088529958	6,305985022	0,000651692	0,044120775
TRAPPC5	TRAPPC5	126003	1,255174908	5,365813481	0,00064266	0,044120775
POLE2	POLE2	5427	1,613851161	0,786138465	0,000650227	0,044120775
ARHGAP22	ARHGAP22	58504	1,79392767	3,710901691	0,000641895	0,044120775
SLC1A7	SLC1A7	6512	3,892893368	3,5706866	0,000655437	0,044162021
MRPL27	MRPL27	51264	0,865953142	5,597995303	0,000661452	0,044355049
EGFR	EGFR	1956	-1,652119901	5,742313586	0,000677446	0,044445341
URB2	URB2	9816	-1,177668165	4,163447778	0,000678579	0,044445341
TRIP11	TRIP11	9321	-0,837590158	4,544861283	0,000670351	0,044445341
COMMD4	COMMD4	54939	0,800359551	6,195192997	0,000669786	0,044445341
GPX1	GPX1	2876	0,9162322	8,769290249	0,000675574	0,044445341
SLC25A35	SLC25A35	399512	0,883144504	2,282362145	0,000693038	0,045141565
PCOLCE	PCOLCE	5118	1,595244612	8,808279661	0,00069562	0,045141565
ASCC3	ASCC3	10973	-0,833344013	5,482195448	0,000710396	0,045580405
BCL2L12	BCL2L12	83596	0,807753213	3,78942136	0,000712217	0,045580405
BLOC1S1	BLOC1S1	2647	0,851719319	6,158736419	0,000712824	0,045580405
DCI	ECI1	1632	0,990046159	5,947175998	0,000715945	0,045580405
RNASEH2A	RNASEH2A	10535	1,046148403	4,860155903	0,000718566	0,045580405
FLVCR1	FLVCR1	28982	-1,076630033	2,211768704	0,000723012	0,045582479
NDUFB11	NDUFB11	54539	1,047892549	6,490129934	0,000725073	0,045582479
C1orf107	UTP25	27042	-0,846400354	4,946745839	0,000728617	0,045601693
POLR1B	POLR1B	84172	-0,817471664	4,831991026	0,000737569	0,045957709
ATF2	ATF2	1386	-1,134148606	4,224950313	0,000752018	0,046093781
HSPBP1	HSPBP1	23640	0,859301539	5,649217197	0,000750114	0,046093781
TREX1	TREX1	11277	0,986719457	4,113022547	0,000750829	0,046093781
LOC282997	LOC282997	282997	1,232736117	1,970744036	0,000752845	0,046093781
COPE	COPE	11316	0,793748354	7,468144593	0,000761861	0,046443842
CAMSAP1L1	CAMSAP2	23271	-0,8020619	6,507250716	0,000768115	0,046623285
COX5B	COX5B	1329	0,976181636	6,923111555	0,000783327	0,047316489
SPRN	SPRN	503542	1,293424904	2,9083426	0,000786256	0,047316489
STBD1	STBD1	8987	-1,566870348	3,538480171	0,000802766	0,047900611
ZNF678	ZNF678	339500	-1,488823696	0,860589978	0,000801286	0,047900611
TM9SF2	TM9SF2	9375	-1,051079222	7,029050612	0,000810817	0,047974452
MND1	MND1	84057	1,287398274	0,835701581	0,000810657	0,047974452

Supplementary Table 1 cont

Gene Symbol	HGNC approved Gene Symbol	ENTREZ ID	logFC	logCPM	PValue	FDR (adjusted Pvalue)
YIF1B	YIF1B	90522	0,825732849	5,763762729	0,000816755	0,048123631
RNF6	RNF6	6049	-0,759134461	4,973747551	0,00082679	0,048511885
NUBP2	NUBP2	10101	0,728046395	5,921723759	0,000831838	0,048605578
SARS2	SARS2	54938	0,813292889	4,30324278	0,00083547	0,04861607
SEL1L	SEL1L	6400	-0,799250127	6,678573577	0,000842129	0,04880192
TCEB2	ELOB	6923	0,990022849	7,322198898	0,000847712	0,04892411
PPP1R15B	PPP1R15B	84919	-1,221789632	6,667635225	0,000859801	0,049174187
SNHG11	SNHG11	128439	0,944053899	3,319851377	0,000859534	0,049174187
AURKB	AURKB	9212	1,651815464	3,463222985	0,000862521	0,049174187
HECTD1	HECTD1	25831	-0,881030935	6,519159851	0,000866928	0,049226139
TGFA	TGFA	7039	-1,875685999	1,803823941	0,000887281	0,049779646
EP300	EP300	2033	-0,8588935	5,749666948	0,000881583	0,049779646
TELO2	TELO2	9894	0,705774735	5,453458771	0,000884795	0,049779646

Supplementary Table 2

Term id	Term Definition	Enrichment	Corrected pvalue
GO:0045333	cellular respiration	10/168	0.0004
GO:0006901	vesicle coating	6/67	0.0013
GO:0051651	maintenance of location in cell	7/94	0.0015
GO:0090114	COPII-coated vesicle budding	6/69	0.0023
GO:0048199	vesicle targeting, to, from or within Golgi	6/70	0.003
GO:0006414	translational elongation	8/125	0.0035
GO:0045930	negative regulation of mitotic cell cycle	14/334	0.0049
GO:0090068	positive regulation of cell cycle process	13/301	0.0053
GO:0048194	Golgi vesicle budding	6/77	0.0066
GO:0009394	2'-deoxyribonucleotide metabolic process	4/31	0.0071
GO:1903358	regulation of Golgi organization	3/15	0.0076
GO:0006281	DNA repair	18/508	0.0083
GO:0007049	cell cycle	36/1316	0.0084
GO:0015980	energy derivation by oxidation of organic compounds	11/237	0.0093
GO:0019692	deoxyribose phosphate metabolic process	4/33	0.0095
GO:0031145	anaphase-promoting complex-dependent catabolic process	6/83	0.0104
GO:0022904	respiratory electron transport chain	7/112	0.0105
GO:0009262	deoxyribonucleotide metabolic process	4/35	0.0109
GO:0045786	negative regulation of cell cycle	20/611	0.012
GO:0010965	regulation of mitotic sister chromatid separation	5/58	0.0126
GO:0000723	telomere maintenance	7/113	0.0133
GO:0006260	DNA replication	10/215	0.0141
GO:0035855	megakaryocyte development	3/17	0.0142
GO:0070125	mitochondrial translational elongation	6/88	0.0142
GO:0042775	mitochondrial ATP synthesis coupled electron transport	6/91	0.0148
GO:0006119	oxidative phosphorylation	7/117	0.0162
GO:0042773	ATP synthesis coupled electron transport	6/92	0.0172
GO:0046825	regulation of protein export from nucleus	4/39	0.0176
GO:0009264	deoxyribonucleotide catabolic process	3/19	0.0185

Supplementary Table 2

Term id	Term Definition	Enrichment	Corrected pvalue
GO:0006974	cellular response to DNA damage stimulus	23/779	0.0188
GO:0022402	cell cycle process	27/958	0.02
GO:0032200	telomere organization	7/126	0.02
GO:0051656	establishment of organelle localization	13/351	0.0203
GO:0006900	vesicle budding from membrane	6/95	0.0205
GO:0051052	regulation of DNA metabolic process	13/348	0.0216
GO:0006415	translational termination	6/97	0.023
GO:0006996	organelle organization	74/3363	0.0238
GO:0000075	cell cycle checkpoint	9/201	0.0246
GO:0051235	maintenance of location	8/163	0.025
GO:0006259	DNA metabolic process	22/744	0.0256
GO:0033047	regulation of mitotic sister chromatid segregation	5/69	0.0259
GO:0006284	base-excision repair	4/43	0.0269
GO:0030219	megakaryocyte differentiation	3/22	0.0274
GO:0070509	calcium ion import	4/44	0.0285
GO:1902961	positive regulation of aspartic-type endopeptidase activity involved in amyloid precursor protein catabolic process	2/7	0.029
GO:0031648	protein destabilization	4/46	0.0302
GO:0045787	positive regulation of cell cycle	14/405	0.0303
GO:0010564	regulation of cell cycle process	23/803	0.0304
GO:0072358	cardiovascular system development	17/527	0.0309
GO:0016241	regulation of macroautophagy	8/171	0.031
GO:0009411	response to UV	7/139	0.0314
GO:0043624	cellular protein complex disassembly	7/137	0.0318
GO:0098751	bone cell development	3/24	0.0325
GO:0033554	cellular response to stress	41/1695	0.0343
GO:0051972	regulation of telomerase activity	4/49	0.0349
GO:0051650	establishment of vesicle localization	8/174	0.0352
GO:2000278	regulation of DNA biosynthetic process	6/110	0.0368
GO:0072359	circulatory system development	24/872	0.0384
GO:1902959	regulation of aspartic-type endopeptidase activity involved in amyloid precursor protein catabolic process	2/9	0.0384
GO:0051276	chromosome organization	28/1068	0.0385
GO:0051726	regulation of cell cycle	31/1221	0.0387
GO:0034644	cellular response to UV	5/79	0.0392
GO:1900101	regulation of endoplasmic reticulum unfolded protein response	3/26	0.0394
GO:0032543	mitochondrial translation	6/112	0.0404
GO:0071902	positive regulation of protein serine/threonine kinase activity	12/335	0.0409
GO:0016310	phosphorylation	33/1326	0.0429
GO:0051648	vesicle localization	8/185	0.0436
GO:0051347	positive regulation of transferase activity	19/652	0.0442
GO:0001944	vasculature development	16/517	0.0442
GO:0033045	regulation of sister chromatid segregation	5/81	0.0444
GO:0031570	DNA integrity checkpoint	7/151	0.0447
GO:0051640	organelle localization	17/564	0.0455
GO:0043618	regulation of transcription from RNA polymerase II promoter in response to stress	6/120	0.0474
GO:0034654	nucleobase-containing compound biosynthetic process	28/1090	0.0475
GO:0021795	cerebral cortex cell migration	4/54	0.0475
GO:0051641	cellular localization	53/2387	0.0487
GO:0000186	activation of MAPKK activity	4/55	0.0487
GO:0046777	protein autophosphorylation	8/191	0.0498

Supplementary Table 3

Term id	Term Definition	Enrichment	Corrected pvalue
GO:0098687	chromosomal region	17/348	0.0027
GO:0005759	mitochondrial matrix	20/470	0.0053
GO:0005694	chromosome	32/1076	0.0073
GO:0000781	chromosome, telomeric region	9/158	0.0081
GO:0044428	nuclear part	98/4553	0.0127
GO:0044427	chromosomal part	28/952	0.0139
GO:0044429	mitochondrial part	30/1055	0.0164
GO:0031981	nuclear lumen	90/4167	0.0186
GO:0098798	mitochondrial protein complex	12/280	0.0228
GO:0035861	site of double-strand break	5/59	0.0242
GO:0016234	inclusion body	6/82	0.0244
GO:0005654	nucleoplasm	77/3524	0.029
GO:0002079	inner acrosomal membrane	2/5	0.0312
GO:0005739	mitochondrion	40/1603	0.0335
GO:0031965	nuclear membrane	12/303	0.037
GO:1902494	catalytic complex	35/1378	0.0413
GO:0031931	TORC1 complex	2/7	0.0422
GO:0090734	site of DNA damage	5/72	0.0461
GO:0000776	kinetochore	7/135	0.0465
GO:0030662	coated vesicle membrane	8/177	0.0481

Supplementary Table 4

Term id	Term Definition	Enrichment	Corrected pvalue
2564830	Cytosolic iron-sulfur cluster assembly	3/13	0.0025
204005	COPII-mediated vesicle transport	6/68	0.0049
1428517	The citric acid (TCA) cycle and respiratory electron transport	10/174	0.0072
163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	8/123	0.0087
611105	Respiratory electron transport	7/100	0.0125
180292	GAB1 signalosome	3/17	0.0144
6799198	Complex I biogenesis	5/55	0.0183
74259	Purine catabolism	3/18	0.0204
162909	Host Interactions of HIV factors	8/131	0.0223
2393930	Phosphate bond hydrolysis by NUDT proteins	2/7	0.0243
69002	DNA Replication Pre-Initiation	6/85	0.025
68882	Mitotic Anaphase	10/200	0.0278
2555396	Mitotic Metaphase and Anaphase	10/201	0.0291
69239	Synthesis of DNA	7/119	0.0354
68867	Assembly of the pre-replicative complex	5/68	0.0361
400253	Circadian Clock	5/70	0.0389
5368287	Mitochondrial translation	6/96	0.0404
68949	Orc1 removal from chromatin	5/71	0.0418
174178	APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1	5/72	0.0473
69306	DNA Replication	7/127	0.0494