

SUPPLEMENTAL MATERIAL

IDH2 inhibition enhances proteasome inhibitor responsiveness in hematological malignancies

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SUPPLEMENTAL MATERIALS AND METHODS

Cell culture conditions and reagents

Human multiple myeloma (MM) cell lines KMM-1, U266, KMM-1^{PIR}, U266^{PIR}, RPMI-8226, KMS-18, KMS-27, SK-MM-1, NCI-H929, CMA-03; human chronic myelogenous leukemia cell line K-562; human mantle cell lymphoma (MCL) cell lines JeKo-1, SP-49, Mino, Granta-519; human Burkitt's lymphoma (BL) cell lines HS-Sultan and Raji were obtained from DSMZ (German Collection of Microorganisms and Cell Cultures, Braunschweig, Germany), ATCC (American Type Culture Collection, Manassas, Virginia, USA), or generated in our lab and authenticated by DNA fingerprinting using GenePrint system (Promega, Madison, Wisconsin, USA). Cell lines were maintained in RPMI 1640 medium (EuroClone, Pero, Italy), supplemented with 2 mM of L-glutamine, 100 U/mL of penicillin, 100 µg/mL of streptomycin (Gibco), 10-20% fetal bovine serum (FBS; Sigma-Aldrich, St. Louis, Missouri, USA), and grown at 37°C in humidified atmosphere with 5% CO₂. CMA-03 cells were supplemented with 10 ng/mL IL-6.¹ 293T cells obtained from DSMZ were cultured under standard conditions (37°C in humidified atmosphere, with 5% CO₂) in DMEM supplemented with 10% FBS. For hypoxic experiments, cells were cultured (24 hours before the treatment and until the end of the experiment) under 1% oxygen concentration using a Hypoxia Chamber (STEMCELL Technologies, Vancouver, Canada). For experiments with glucose deprivation, RPMI 1640 medium without glucose (Corning New York, USA), supplemented with 100 U/mL of penicillin, 100 µg/mL of streptomycin (Gibco), and 10% FBS was used. Cells were seeded at 1-2 x 10⁵ cells/mL before treatments. Peripheral blood mononuclear cells (PBMCs) from healthy blood donors were provided by the local Blood Bank (Fondazione Strumia) and isolated on a Ficoll-Hypaque density gradient. Bone marrow white cells (containing more than 20% of myeloma cells) were obtained from routine BM aspirates of myeloma patients. They were collected by buffy coat, incubated with Red Blood Cell Lysing Buffer (Sigma), suspended in RPMI-10% FBS medium and seeded (10⁶ cells/mL) on a 50% confluent HS-5 cell monolayer. Informed consent was obtained from all enrolled patients after the procedures were approved by the local ethical committee. Carfilzomib (PR-171), AGI-6780, and 3-TYP were obtained from Selleckchem (Munich, Germany), bortezomib (PS-341) from Millennium Pharmaceuticals (Cambridge, Massachusetts, USA), ixazomib (MLN9708) and Nampt-IN-1 from MedChemtronica (Stockholm, Sweden), FK866 and GMX-1778 from Sigma, and AGK7 from Cayman Chemical (Ann Arbor, Michigan, USA).

shRNA screening

The shRNA library targeting 152 cancer driver genes (supplemental Table S1) was assembled with 684 lentiviral shRNA (pLKO backbone) from The RNAi consortium (TRC - <https://www.broadinstitute.org/rnai-consortium/rnai-consortium-shrna-library>)

(supplemental Table S2). Lentiviral infections were optimized in U bottom 96-well plates for growth conditions, plate types, viral dose, and assay time points. KMM-1^{PIR} cells were seeded at a density of 20 000 cells/well, incubated for 24 hours, and infected using viral volumes of shRNA lentiviral supernatants sufficient to transduce 30% of cells (day -3). After 24h the cells were selected with puromycin (2.5 µg/mL) (day -2). Infected cells were detected using Cell Titer Glo (Promega) luminescence assay performed in duplicate two days after selection (day 0). Percentage of transduction (T) was defined as: (average luminescence value of puromycin selected samples/average luminescence of unselected samples) x 100 (supplemental Table S4). As controls, we used samples infected with different doses of empty shRNA (CTRL_PURO), non-targeting shRNA (CTRL_67C), GFP empty vector (CTRL_GFP), or non-infected cells (NT) with or without puromycin selection (supplemental Table S4). Samples with T<10% were excluded from subsequent analysis. At day 0 KMM-1^{PIR} cells were splitted and treated with 2.5 nM carfilzomib (CFZ) or with control diluent (DMSO) every 72 hours. Cell Titer Glo was performed 3 and 7 days post-treatment. Luminescence value were used to calculate Cell Growth (CG), Growth Rate (GC), and Z-Score for each time point. CG was calculated as the ratio between day 3 (or day 7) and day 0 luminescence values, adjusted for dilution factor. GR was calculated as follow: $GR = (CG_{shRNA\ infected\ cells} / CG_{control\ cells}) \times 100$ (supplemental Table S5). Z-score was calculated using the following formula: $Z = (X - \mu) / \sigma$; X: GR at given time point (day 3 or day 7); μ : average GR of controls; σ : standard deviation of controls (supplemental Table S6). We selected samples with Z-score lower than -0.75 (162 shRNAs) at day 3, and -0.8 (195 shRNA) at day 7. Within these groups candidate genes were selected according to the following criteria: more than one shRNA sequence per gene determine growth inhibition in presence of CFZ; shRNA reduces target gene expression by at least 60%; positive hits are present both at day 3 and day 7 (19 genes), or within the top 5 at day 7 (5 genes) (Supplemental Table S7). Top 24 scoring genes were validated in U266^{PIR} cell line using similar protocol for the primary screening, scaled up to 6 cm dishes (data not shown; Figure 1C). Correlation analysis between gene silencing and phenotype was used to define top three candidates.

Virus production and in vitro transduction

High titer lentiviral stocks were produced in 293T cells by co-transfecting the expression vector (in pLKO, pCW57.1, pLX304, pLVTHM backbones) and packaging vectors (pCMV-dR8.74, VSV-G/pMD2.G) with the Effectene Transfection Reagent (Qiagen, Milan, Italy), according to the manufacturer's instructions. Supernatants were harvested over 36 to 60 hours, filtrated (0.22 μm pore), and used directly. Aliquots of virus, plus 4-8 $\mu\text{g}/\text{mL}$ polybrene, were used to infect KMM-1, KMM-1^{PIR}, U266, U266^{PIR}, and KMS-27 cells ($1 \times 10^5/\text{mL}$). Fresh medium was supplemented 2 hours after infection.

SIRT3 construct

pCW57.1-SIRT3-FLAG vector was constructed by replacing the Cas9 of the pCW57.1-Cas9 vector (Addgene plasmid # 50661) with the SIRT3-Flag cassette from pcDNA3.1+ (Addgene plasmid # 13814), using the NheI-BamHI sites. Stable cell lines expressing the construct were selected by treatment with 2 $\mu\text{g}/\text{mL}$ puromycin (Sigma-Aldrich) for 24 hours. SIRT3 expression was induced by doxycycline treatment (1 $\mu\text{g}/\text{mL}$) for 72h.

IDH2 construct

IDH2 was amplified by PCR from KMM-1^{PIR} using specific primers and cloned into pENTR1A no ccdB vector (Eric Campeau, <http://ericcampeau.com/>). Lentiviral expression vector pLX304-IDH2-FLAG was generated by Gateway recombination (Gateway System, Invitrogen). KMM-1^{PIR} cells expressing the construct were selected by treatment with 7.5 $\mu\text{g}/\text{mL}$ blasticidin (Sigma-Aldrich) for 48 hours.

Inducible shIDH2

pLVTHM-GFP-shIDH2 vector was constructed by subcloning the U6 promoter–shIDH2-A4 cassette into the EcoRI-ClaI sites of the pLVTHM vector,² kindly provided by D. Trono (University of Geneva, Geneva, Switzerland). For conditional RNAi, KMS-27 cells were transduced at high efficiency with pLV-DsRed-tTRKRAB plasmid, expanded, and used for transduction with pLVTHM-GFP-shIDH2 lentiviral particles. Next, cells were treated with doxycycline (1 $\mu\text{g}/\text{mL}$) for 12 hours to induce shIDH2 expression, double GFP⁺DsRed⁺ cells were flow sorted (FACS Aria III, BD Biosciences, San Jose, California, USA) and expanded.

shSIRT3

Five different shRNAs glycerol stocks were purchased (Sigma-Aldrich: TRCN0000331109, TRCN0000038893, TRCN0000038892, TRCN0000038890, TRCN0000038889). High titer lentiviral stocks were produced as described above. Stable cell lines expressing the shRNA were selected by treatment with 2 $\mu\text{g}/\text{mL}$ puromycin for 24 hours.

Purification of total RNA and Reverse Transcription-quantitative Polymerase Chain Reaction (RT-qPCR)

Total RNA was extracted using Magmax 96 Total RNA isolation kit (Ambion) or RNeasy Mini Kit (Qiagen) according to the manufacturer's instructions. cDNA was obtained from total RNA, previously treated with RQ1 RNase-free DNase (Promega), using iScript RT (Bio-Rad Laboratories, Richmond, CA) or Superscript III reverse transcriptase (Invitrogen, Carlsbad, CA), following the manufacturer's instructions. Quantitative PCR reactions were performed in 384-well plates with a Thermal iCycler (Bio-Rad Laboratories, Hercules, CA; USA) using the Bio-Rad iQ SYBR Green Supermix according to the manufacturer's instructions. The PCR cycling conditions were as follows: 95°C for 5 minutes followed by 40 cycles at 94°C for 10 seconds and 60°C for 30 seconds. The oligonucleotide primer pairs used for RT-qPCR were designed with PrimerBLAST (<http://www.ncbi.nlm.nih.gov/tools/primer-blast/>), and available upon request. To confirm the amplification specificity, the PCR products were subjected to the analysis of melting curve. All PCR assays were performed in triplicate and the average Ct (cycles to threshold) was used for the comparative Ct method.³ Quantification of GAPDH levels served as an endogenous control. Control infections with scrambled shRNA, empty vector, or non-infected cells were used to define 100% expression.

DNA sequencing

Genomic DNA of KMM-1, U266, KMM-1^{PIR}, and U266^{PIR} cell lines was extracted using DNeasy Blood & Tissue Kit (Qiagen). Exon 4 of the *IDH2* gene was analyzed by PCR amplification and bidirectional direct sequencing using the ABI PRISM 3100 Genetic Analyzer (Applied Biosystems, Foster City, California, USA). Primer sequences are available upon request.

Western Blotting

Protein extracts were prepared using Lysis Buffer containing 20 mM Tris-HCl (pH 7.4), 150 mM NaCl, 5 mM EDTA, 1% Triton X-100, 1 mM PMSF, 10 mM NaF, 1 mM Na₃VO₄, and Protease Inhibitor Cocktail (Roche, Basilea, Switzerland). Total protein concentrations were measured using Bio-Rad DC protein assay kit (Bio-Rad). Equal amounts of protein lysates were resolved by SDS-PAGE, transferred to nitrocellulose membrane, and probed with the following primary antibodies: rabbit PARP-1 (H-250; sc-7150, Santa Cruz Biotechnology, Dallas, Texas, USA), mouse actin (clone C4; MAB1501, Merck Millipore, Burlington, Massachusetts, USA), mouse ubiquitin (13-1600, Zymed), mouse IDH2 (ab55271, Abcam, Cambridge, UK), mouse vinculin (SAB4200080, Sigma), mouse cycline

E (HE12; sc-247, Santa Cruz Biotechnology), rabbit cyclin A (H-432; sc-751, Santa Cruz Biotechnology), rabbit cyclin B1 (H433; sc-752, Santa Cruz Biotechnology), mouse p21 (610233, BD Biosciences), mouse p27 (610241, BD Biosciences), rabbit cleaved PARP-1 (5625, Cell Signaling Technology, Leiden, The Netherlands), rabbit cleaved caspase-9 (7237, Cell Signaling Technology), rabbit cleaved caspase-7 (8438, Cell Signaling Technology), rabbit cleaved caspase-3 (9664, Cell Signaling Technology), rabbit sirtuin 3 (D22A3; 5490, Cell Signaling Technology), mouse α -tubulin (clone B-5-1-2, T5168, Sigma).

Gene Expression Profiling

Total RNA samples were processed according to manufacturer's procedure for global gene expression profiling onto GeneChip[®] Human Gene 2.0 ST arrays (Affymetrix Inc., Santa Clara, CA). Normalized expression values were obtained using Robust Multi Array Average (RMA) procedure. A custom annotation pipeline was applied that combined GENCODE v25 (Ensembl v87) annotations with the CDF (Chip Definition File) version 21 for gene annotations freely available at <http://brainarray.mbni.med.umich.edu/Brainarray/Database/CustomCDF/21.0.0/genecodeg.asp>. The expression levels of 18642 Ensembl genes were obtained. Probes mapping to regions with ambiguous detection due to transcript overlapping were discarded. Hierarchical agglomerative clustering based on the most variable genes (genes whose average change in expression levels varied at least two fold from the mean across the entire panel) was performed using Pearson's correlation and average as distance and linkage methods, respectively, by means of DNA-Chip Analyzer software.⁴ Supervised analyses were carried out using the Significant Analysis of Microarrays software version 5.00⁵ using the web application provided in the shiny package of the R software (<https://github.com/MikeJSeo/SAM>). The cut-off point for statistical significance (at a q-value 0) was determined by tuning the Δ parameter on the false discovery rate and controlling the q-value of the selected probes. Functional annotation clustering using DAVID 6.8 (<https://david.ncifcrf.gov/>) was applied at high stringency on gene-ontology terms and significant clusters (Enrichment Score, ES>1.3) were selected for each list of differentially expressed genes.

Analysis of apoptosis and cell cycle

Apoptosis was measured by flow cytometry after staining with tetramethylrodamine methyl ester (TMRM; Molecular Probes, Eugene, Oregon, USA) or Annexin V-FITC Kit (Miltenyi Biotec, Bergisch Gladbach, Germany), according to the manufacturer's instructions.

CD138⁺ cells were identified by anti hCD138-FITC antibodies (clone: 44F9; 130-098-197, Miltenyi Biotec). Cell cycle was measured by propidium iodide (PI) staining - flow cytometry. Briefly, cells were washed in PBS, treated with RNase (0.14 mg/mL) and incubated with propidium iodide (28.57 µg/mL). Data were acquired using FACSCanto II cytofluorimeter and processed with FACSDiva 8.0 software (BD Biosciences).

Reactive oxygen species (ROS) production

ROS production was detected by flow cytometry using 20 µM 2',7'-Dichlorofluorescein diacetate (Sigma-Aldrich) incubated for 30 minutes at 37°C. Mitochondrial ROS production was detected by flow cytometry using the MitoSOX Red mitochondrial superoxide indicator (Thermo Fisher Scientific, Waltham, Massachusetts, USA), according to the manufacturer's instructions.

Mitochondria isolation

To isolate mitochondrial fractions, cells were washed twice in ice-cold PBS, then lysed in 0.5 mL mitochondria lysis buffer (50 mM Tris, 100 mM KCl, 5 mM MgCl₂, 1.8 mM ATP, 1 mM EDTA pH 7.2), supplemented with protease inhibitor cocktail III (Calbiochem), 1 mM PMSF, and 250 mM NaF. Samples were clarified by centrifuging at 650 × g for 3 min at 4°C; the supernatant was collected and centrifuged at 13 000 × g for 5 min at 4°C. The cytosolic extract was transferred to a new series of tubes and stored at -80°C after protein quantification. The pellet containing mitochondria was washed once with lysis buffer and re-suspended in 0.25 mL mitochondria resuspension buffer (250 mM sucrose, 15 mM K₂HPO₄, 2 mM MgCl₂, 0.5 mM EDTA). A 50 µL aliquot was sonicated and used for the measurement of protein content.

NF-κB activity

Protein extracts were prepared using Lysis Buffer containing 20 mM Tris-HCl (pH 7.4), 150 mM NaCl, 5 mM EDTA, 0.1% Triton X-100, 1 mM PMSF, 10 mM NaF, 1 mM Na₃VO₄, and Protease Inhibitor Cocktail (Roche). NF-κB activity was assessed using the TransAM™ Flexi NF-κB Family kit (Active Motif, Carlsbad, California, USA). Briefly, total protein extracts (5 µg) were incubated with biotinylated probe containing the κB consensus site 5'-GGGACTTTCC-3' (1 pmol). Binding of NF-κB subunits to the κB target sites was detected using specific primary antibodies against NF-κB p50, p52, p65, c-Rel, and RelB, according to the manufacturer's instructions. Absorbance at 450 nm was measured with a Packard EL340 microplate reader (Bio-Tek Instruments, Winooski, Vermont, USA). For each set of experiments, a blank was prepared with bi-distilled water, and its absorbance was

subtracted from that obtained in the presence of protein extracts. Data obtained are absorbance units·mg⁻¹ cell proteins.

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SUPPLEMENTAL FIGURES AND LEGENDS

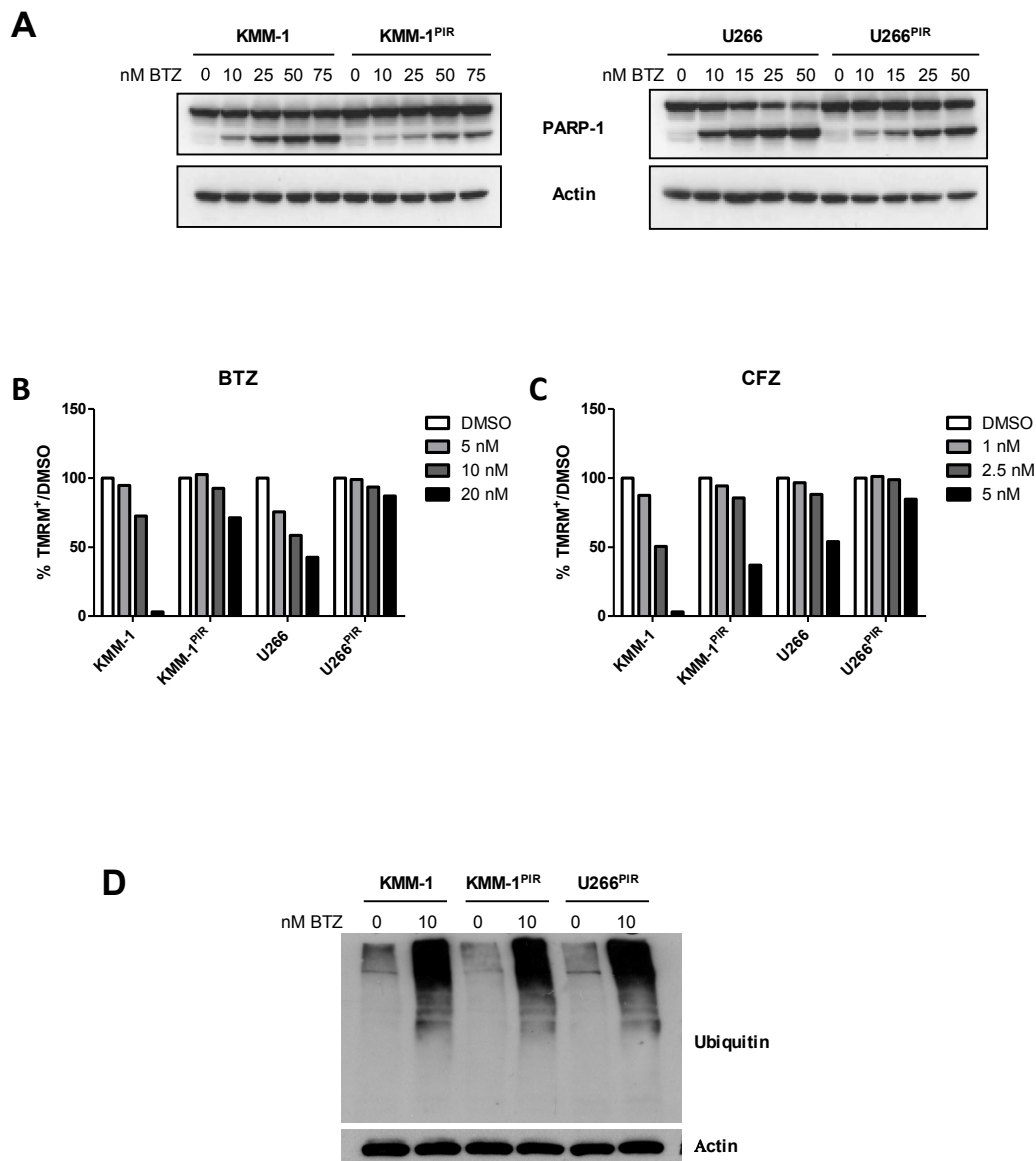


Figure S1. The multiple myeloma cell lines KMM-1^{PIR} and U266^{PIR} are cross-resistant to the proteasome inhibitors bortezomib (BTZ) and carfilzomib (CFZ). KMM-1^{PIR} and U266^{PIR} cells were generated from the parental cell lines cultured in presence of increasing concentrations of BTZ. **(A)** KMM1, KMM-1^{PIR}, U266, and U266^{PIR} cells were treated with the indicated concentrations of BTZ. Levels of PARP-1 cleavage were analyzed by western blotting 24 hours post-treatment. Actin protein expression was included for protein loading normalization. **(B-C)** KMM1, KMM-1^{PIR}, U266, and U266^{PIR} cells were treated with the indicated concentrations of BTZ or CFZ. Cell viability was measured by TMRM staining-flow cytometry 72 hours post-treatment. **(D)** KMM-1, KMM-1^{PIR}, and U266^{PIR} cell lines were treated with control solvent (DMSO) or BTZ (10 nM) for 24 hours. Accumulation of ubiquitinated proteins induced by proteasome inhibition was assayed by western blotting with anti-ubiquitin antibody. Actin protein expression was included for protein loading normalization.

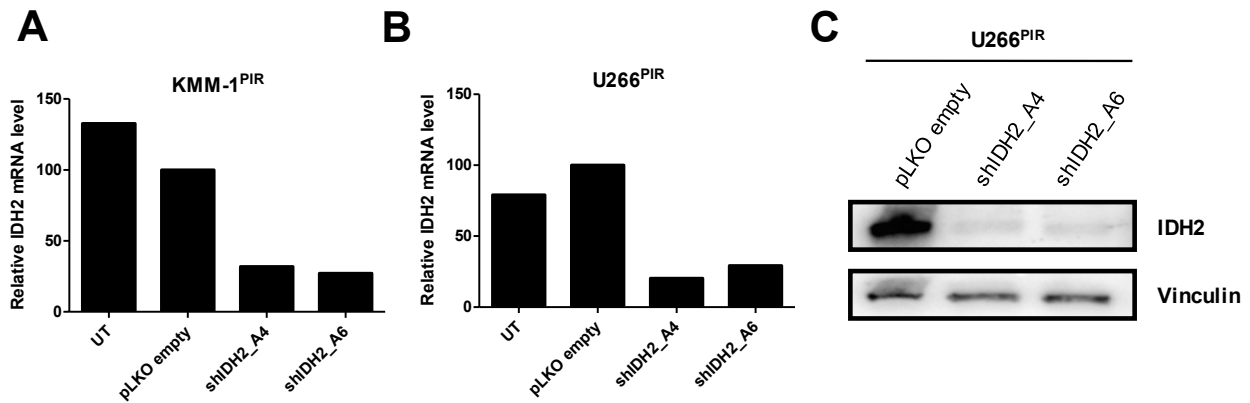


Figure S2. (A) KMM-1^{PIR} and (B) U266^{PIR} cells were transduced with lentiviral particles expressing two shRNAs (shIDH2_A4, shIDH2_A6) targeting IDH2, empty vector (pLKO empty), or left untransduced (UT). IDH2 silencing was monitored by RT-qPCR after puromycin selection. (C) Representative western blot showing IDH2 expression levels in U266^{PIR} cells transduced with lentiviral particles expressing the empty vector (pLKO empty) or the shRNAs targeting IDH2: shIDH2_A4 and shIDH2_A6. Vinculin protein expression was included for protein loading normalization.

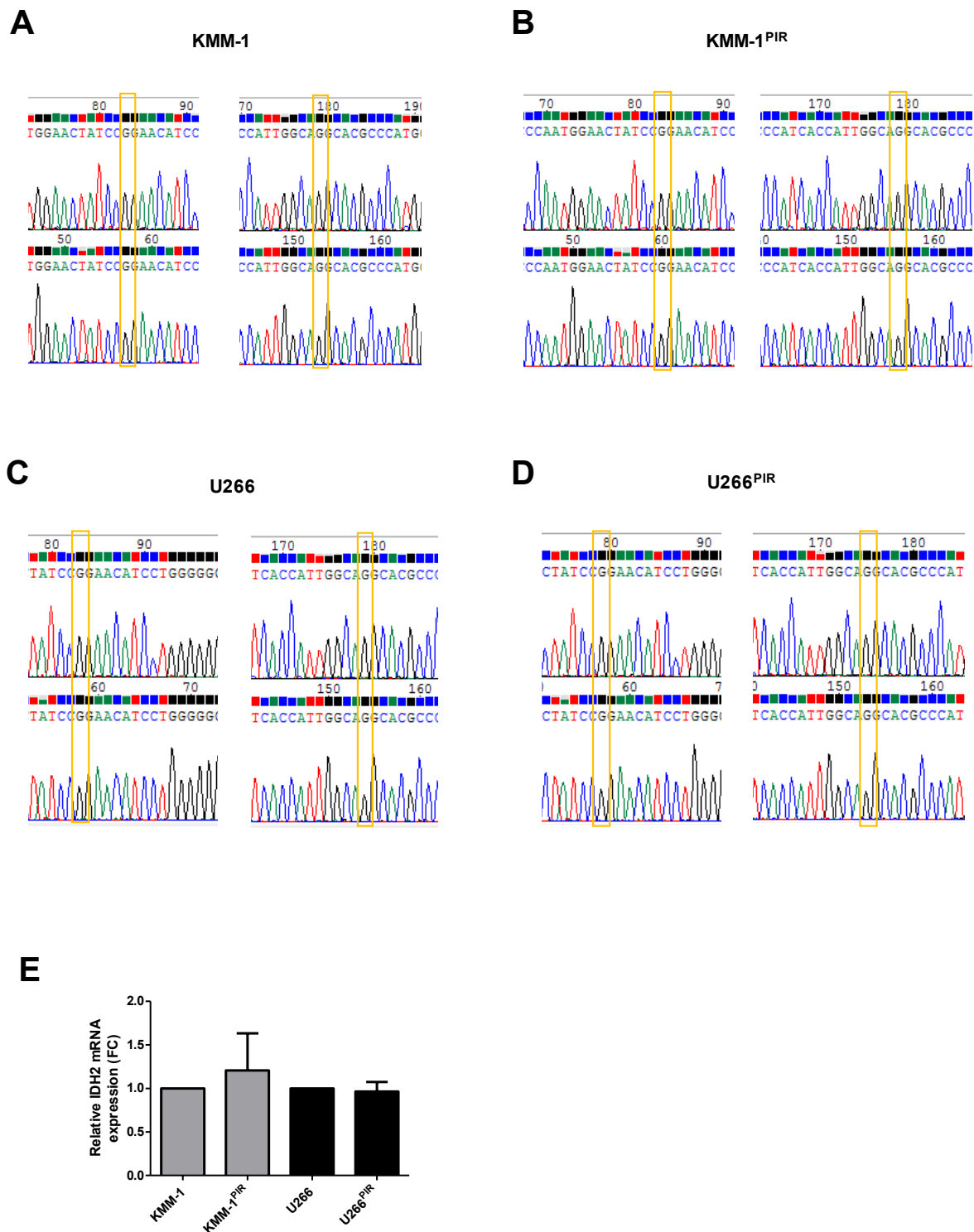


Figure S3 (A-D) Sanger-sequencing showing wild-type *IDH2* codon 140 (CGG, R140) and wild-type *IDH2* codon 172 (AGG, R172) of (A) KMM-1, (B) KMM-1^{PIR}, (C) U266, and (D) U266^{PIR} cells (yellow rectangles). **(E)** *IDH2* mRNA expression levels monitored by RT-qPCR in KMM-1, KMM-1^{PIR}, U266, and U266^{PIR} cells. Data are represented as fold change (FC) over the sensitive counterpart.

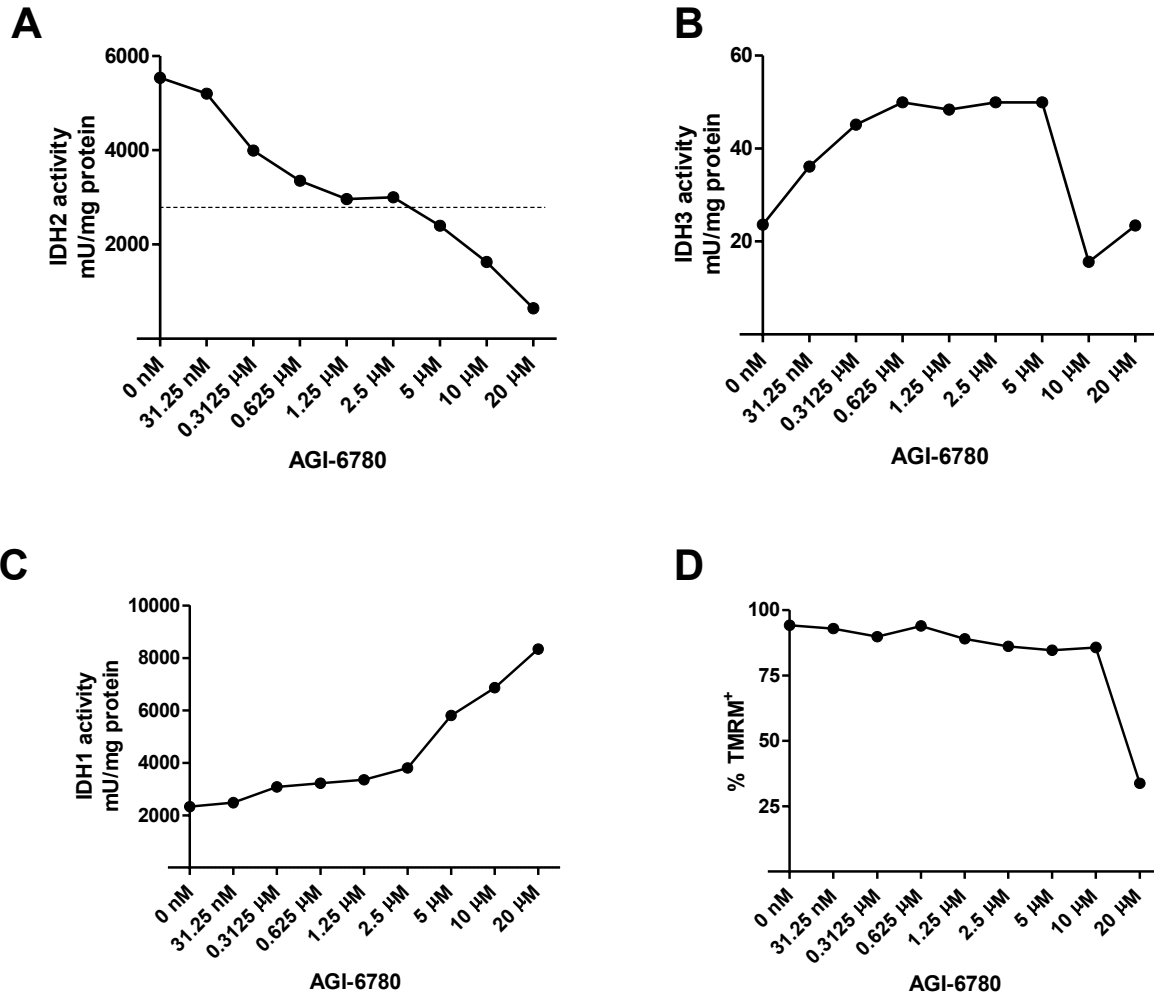


Figure S4. KMS-27 treated with increasing doses of AGI-6780 were analyzed for **(A)** IDH2, **(B)** IDH3, **(C)** IDH1 activity 6 hours post-treatment, **(D)** and for cell viability measured by TMRM staining-flow cytometry 48 hours post-treatment.

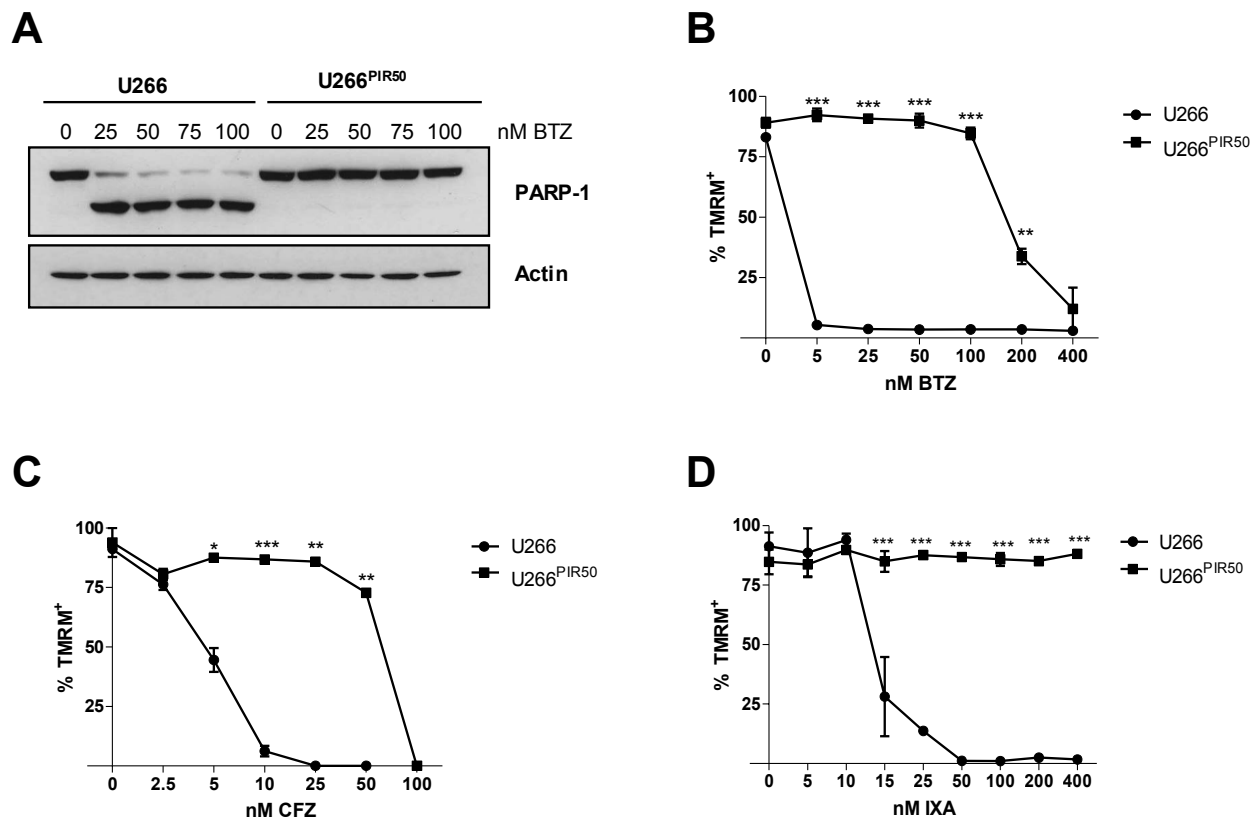


Figure S5. U266^{PIR50} cells were generated from U266 cultured in presence of increasing concentrations of BTZ. **(A)** U266 and U266^{PIR50} cells were treated with the indicated concentrations of BTZ. Levels of PARP-1 cleavage were analyzed by western blotting 24 hours post-treatment. Actin protein expression was included for protein loading normalization. **(B-D)** U266 and U266^{PIR50} cells were treated with the indicated concentrations of (B) BTZ, (C) CFZ, or (D) ixazomib (IXA). Cell viability was measured by TMRM staining-flow cytometry 72 hours post-treatment. Data are the means \pm s.d. of three, two, and five independent experiments, respectively (* $P < .05$; ** $P < .01$; *** $P < .001$).

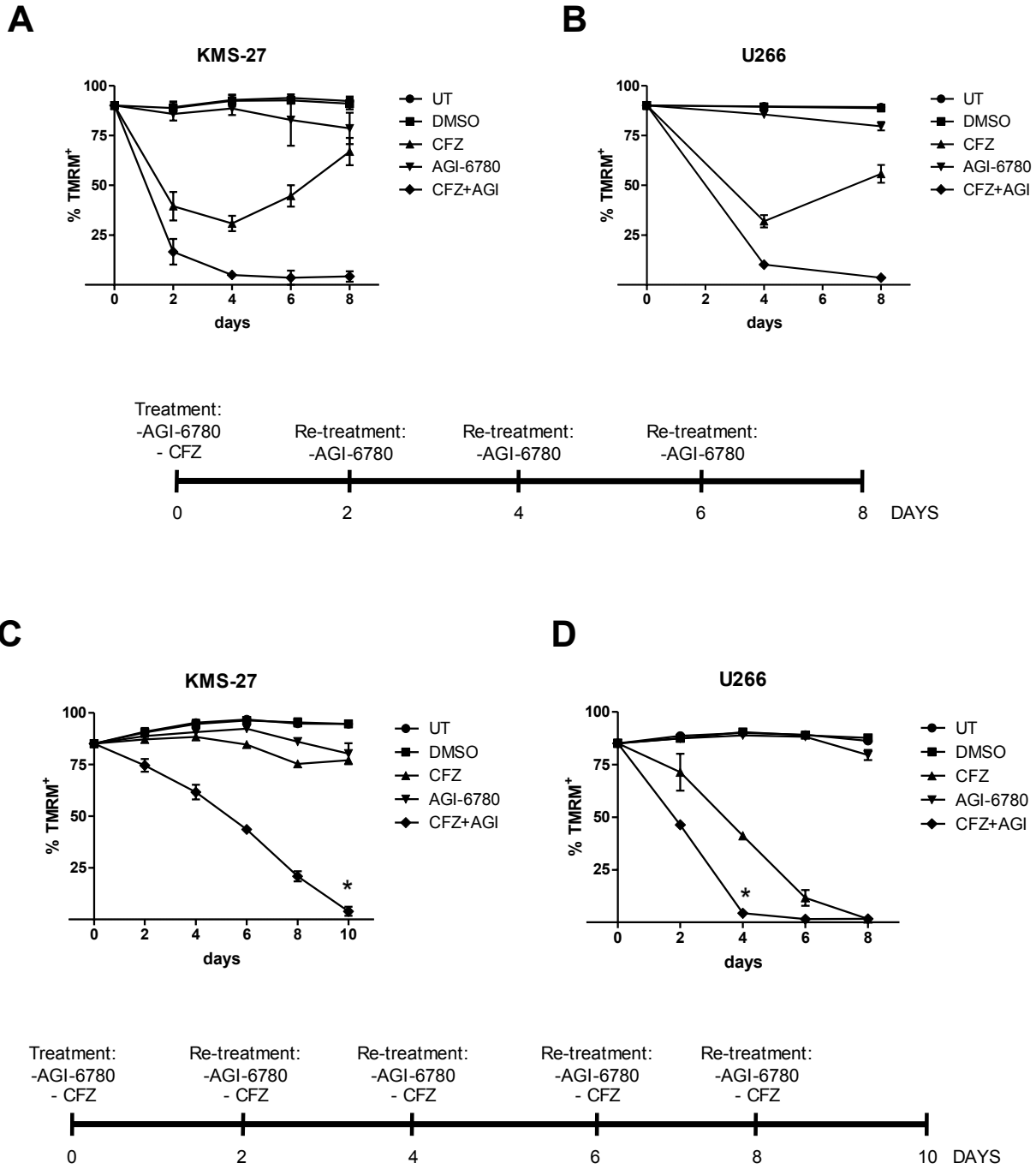


Figure S6. (A-B) KMS-27 and U266 cells were left untreated (UT), treated with DMSO, CFZ (2.5 nM and 5 nM, respectively; single administration), AGI-6780 (5 μ M; every 48 hours), or the combination of the two drugs. Cell viability was measured by TMRM staining-flow cytometry at the indicated time points. Data are the means \pm s.d. of three independent experiments. **(C-D)** KMS-27 and U266 cells were treated with sub-lethal concentrations of CFZ (1.25 or 2.5 nM CFZ, respectively) in combination or not with 5 μ M AGI-6780. Drugs were administered every 48h. Cell viability was measured by TMRM staining-flow cytometry at the indicated time points. Data are the means \pm s.d. of two independent experiments (* P <.05).

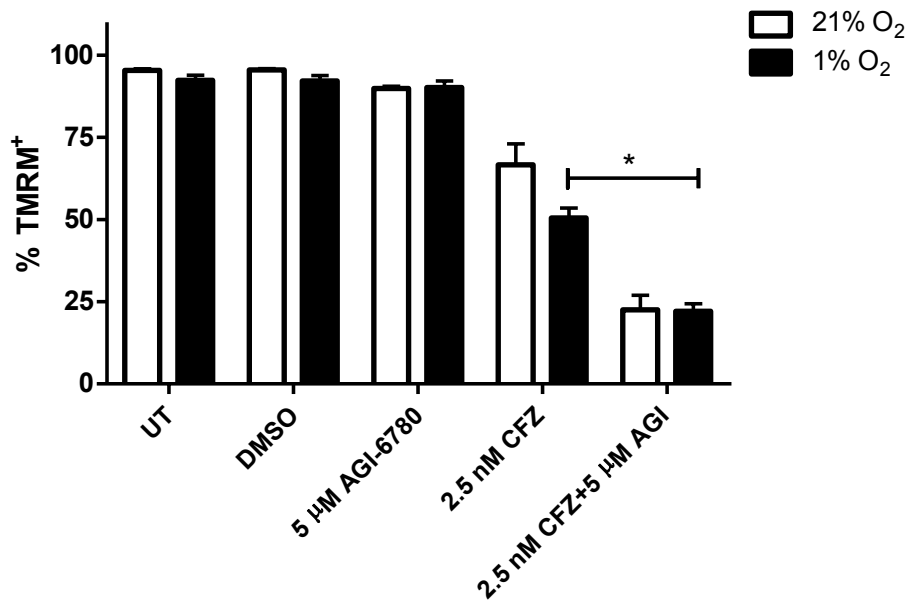
A

Figure S7. KMS-27 were cultured in normoxic (21% O₂) or hypoxic (1% O₂) conditions for 24 hours. Then, cells were treated with DMSO, CFZ (2.5 nM; every 48 hours), AGI-6780 (5 μM; every 48 hours), or the combination of the two drugs. Cell viability was measured by TMRM staining-flow cytometry 96 hours post-treatment. Data are the means ± s.d. of three independent experiments (**P*<.05).

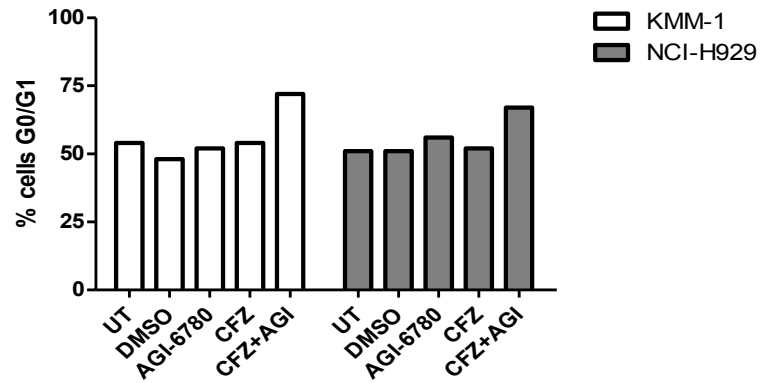
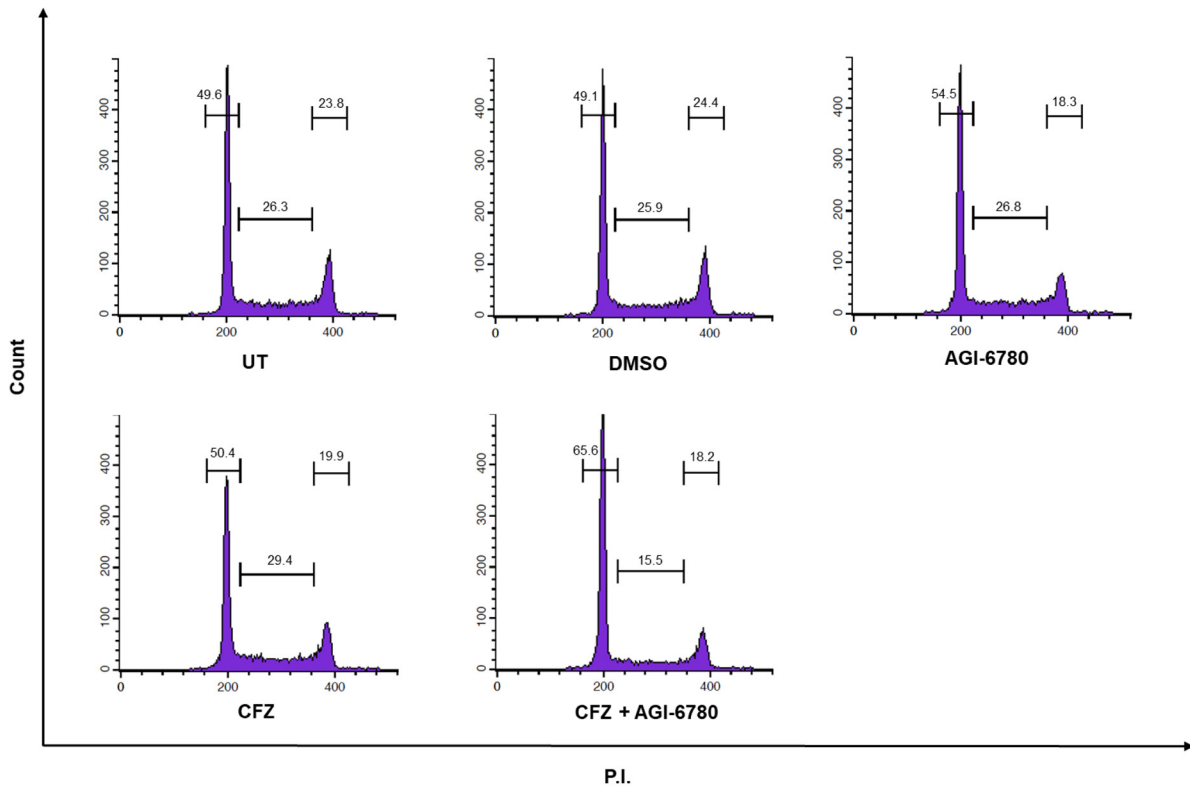
A**B**

Figure S8. A. KMM-1 and NCI-H929 cell lines were treated with AGI-6780 (5 μ M and 10 μ M, respectively) in combination or not with CFZ (5 nM and 2.5 nM, respectively). Cell cycle was measured by flow cytometry 24 hours post-treatment. **B.** Representative cell cycle of NCI-H929 treated with AGI-6780 (10 μ M) in combination or not with CFZ (2.5 nM). Cell cycle was measured by flow cytometry 24 hours post-treatment.

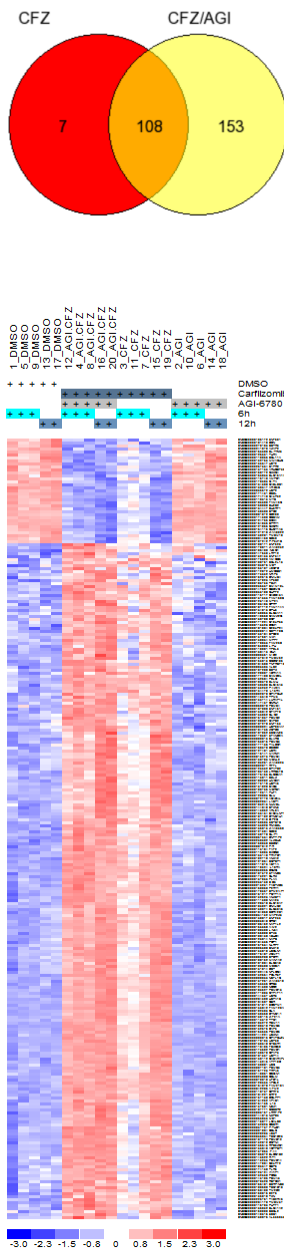
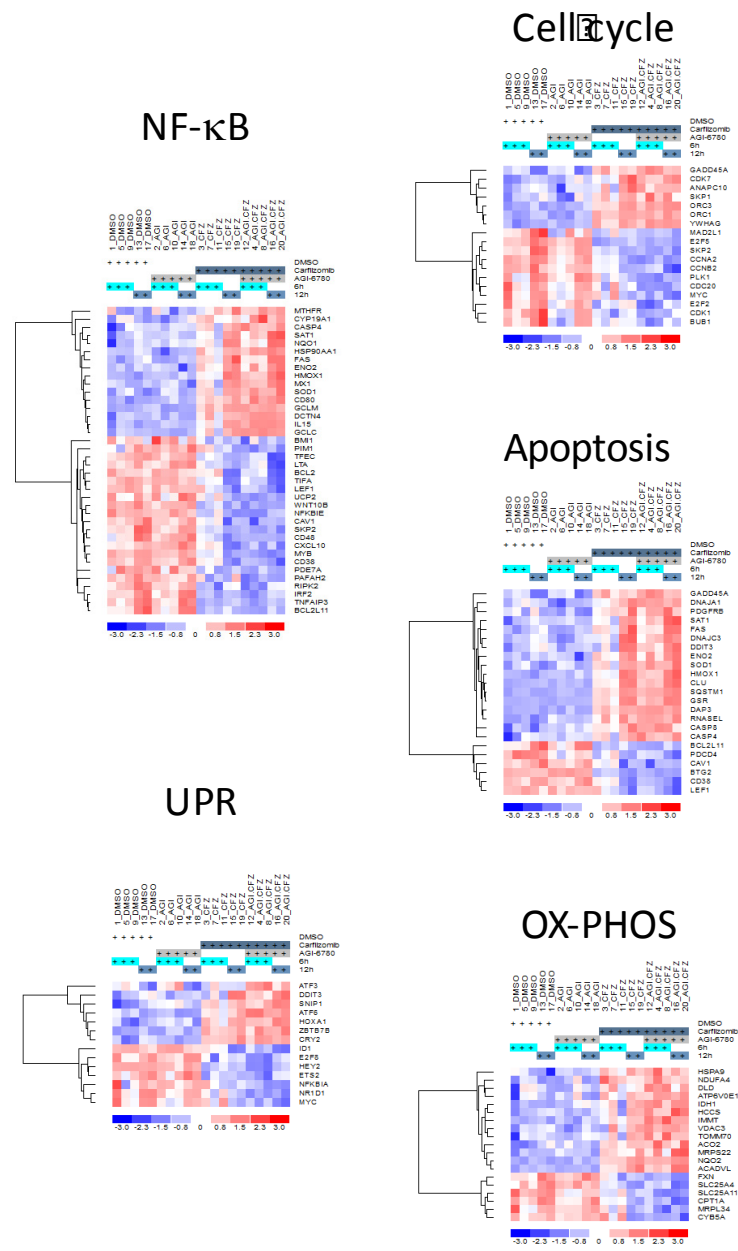
A**B**

Figure S9. Gene expression profile analysis of MM cells treated with CFZ, AGI-6780, or the combination of the two drugs. (A) KMS-27 cells were treated with DMSO, CFZ (2.5 nM), AGI-6780 (5 μ M), or the combination of the two drugs and analyzed 6 (n = 3) and 12 hours (n = 2) post-treatment using GeneChip[®] Human Gene 2.0 ST arrays. Expression values were normalized by Robust Multi Array Average (RMA) procedure and supervised analyses carried out using the Significant Analysis of Microarrays software (q-value = 0). (Upper panel) Venn diagram obtained overlapping genes modulated by CFZ (115) or CFZ/AGI-6780 (261) treatments. (Lower panel) Eisen plot of the expression values of 261 transcripts modulated by CFZ/AGI-6780 treatment. (B) Functional stratification of CFZ/AGI-6780-regulated genes. Genes differentially expressed in KMS-27 cells were grouped according to their functional categories. Pathway analyses of classical PI3 targets such as unfolded protein response (UPR), NF- κ B, cell cycle, apoptosis, and oxidative phosphorylation (OX-PHOS) were affected in response to CFZ alone and these effects were enhanced by the combination with AGI-6780.

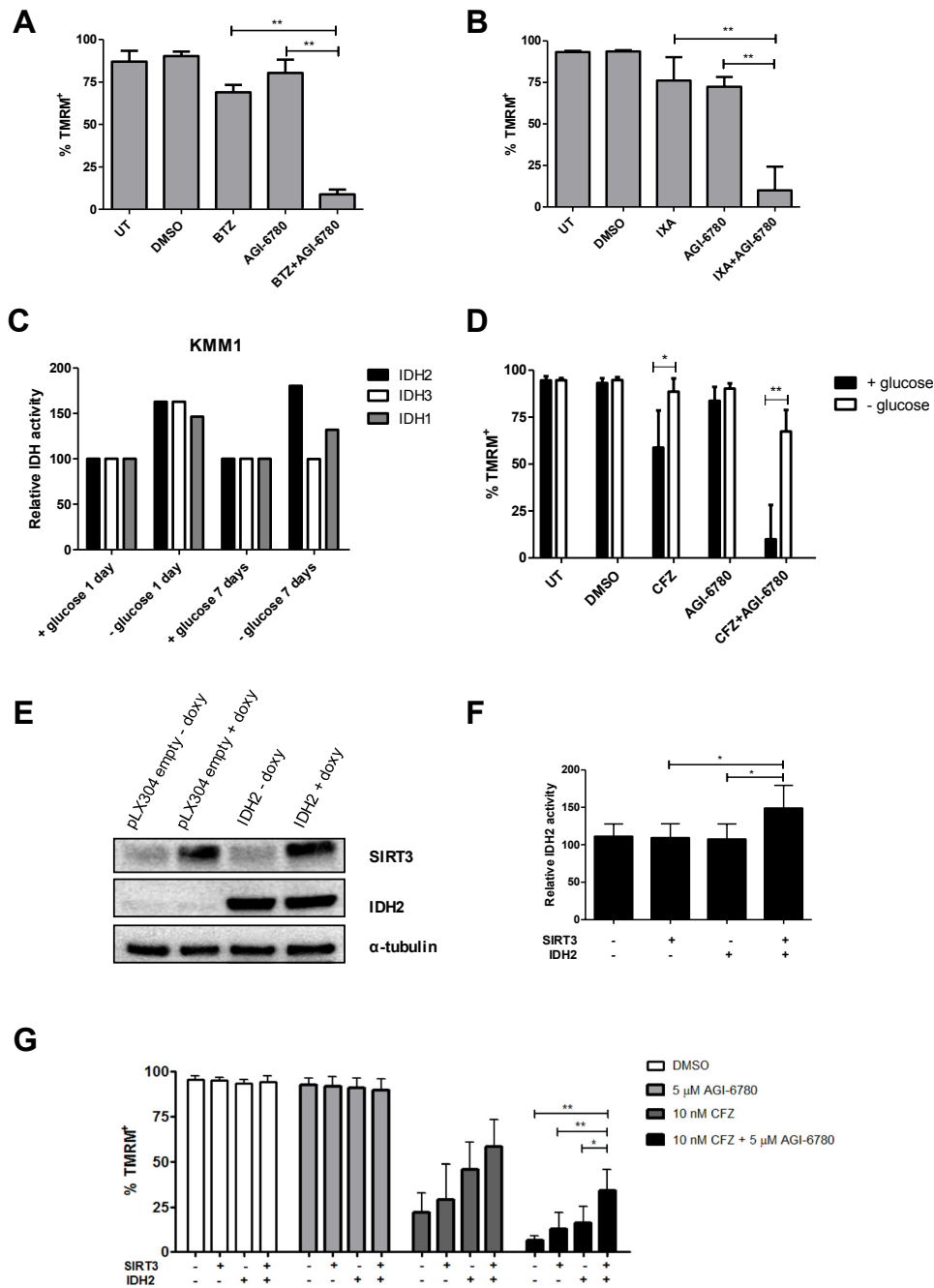


Figure S10. IDH2 inhibition synergizes with first- and second-generation PIs in B-cell hematological malignancies. (A) KMS-27 cells were left untreated (UT), treated with DMSO, bortezomib (BTZ; 3 nM; single administration), AGI-6780 (5 μM; every 48 hours), or the combination of the two drugs. Cell viability was measured by TMRM staining-flow cytometry 10 days post-treatment. Data are the means ± s.d. of three independent experiments. (B) KMS-27 cells were left untreated (UT), treated with DMSO, ixazomib (IXA; 12.5 nM; single administration), AGI-6780 (5 μM; every 48 hours), or the combination of the two drugs. Cell viability was measured by TMRM staining-flow cytometry 10 days post-treatment. Data are the means ± s.d. of three independent experiments. (C) KMM-1 cells were cultured in absence or presence of glucose in the medium for 7 days. IDH1, IDH2, and IDH3 activities were measured after 1 and 7 days of starvation. (D) KMM-1 cells were plated in presence or absence of glucose for 24 hours and left untreated (UT), treated with DMSO, CFZ (2.5 nM), AGI-6780 (5 μM), or the combination of the two drugs.

Cell viability was measured by TMRM staining-flow cytometry 48 hours post-treatment. Data are the means \pm s.d. of five independent experiments. **(E)** Representative western blot showing SIRT3 and IDH2 expression levels in KMM-1^{PIR} cells transduced with lentiviral particles expressing: pLX304-empty vector, pLX304-IDH2-FLAG, pCW57.1-SIRT3-FLAG. The expression of SIRT3 was induced by 72 hours of doxycycline administration. α -tubulin protein expression was included for protein loading normalization. **(F)** IDH2 activity was measured in KMM-1^{PIR} cells 72 hours after doxycycline administration. Data are the means \pm s.d. of four independent experiments. **(G)** KMM-1^{PIR} cells expressing doxycycline-inducible SIRT3 and constitutively expressing IDH2 or empty vector control were treated with DMSO, CFZ (10 nM), AGI-6780 (5 μ M), or the combination of the two drugs. Cell viability was measured by TMRM staining-flow cytometry 48 hours post-treatment. Data are the means \pm s.d. of four independent experiments (* P <.05; ** P <.01; *** P <.001).

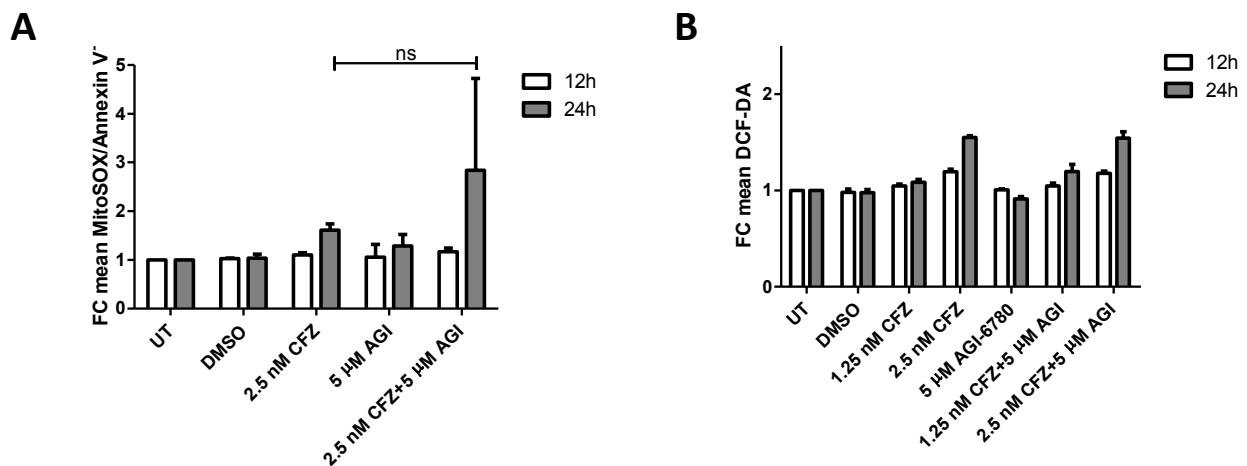


Figure S11. Reactive oxygen species (ROS) concentration in MM cells treated with CFZ/AGI-6780 combination. (A) KMS-27 cells were left untreated (UT), treated with DMSO, CFZ (2.5 nM), AGI-6780 (5 μ M), or the combination of the two drugs. Mitochondrial ROS concentration was measured in viable cells by MitoSOX/Annexin V staining-flow cytometry. MitoSOX mean fluorescence intensities are represented as fold change (FC) over UT cells 12 and 24 hours post-treatment. Data are the means \pm s.d. of three independent experiments. **(B)** KMS-27 cells treated as described above were analyzed for intracellular ROS by 2',7'-Dichlorofluorescein diacetate (DCF-DA) staining-flow cytometry and represented as fold change (FC) over UT cells 12 and 24 hours post-treatment. Data are the means \pm s.d. of two independent experiments.

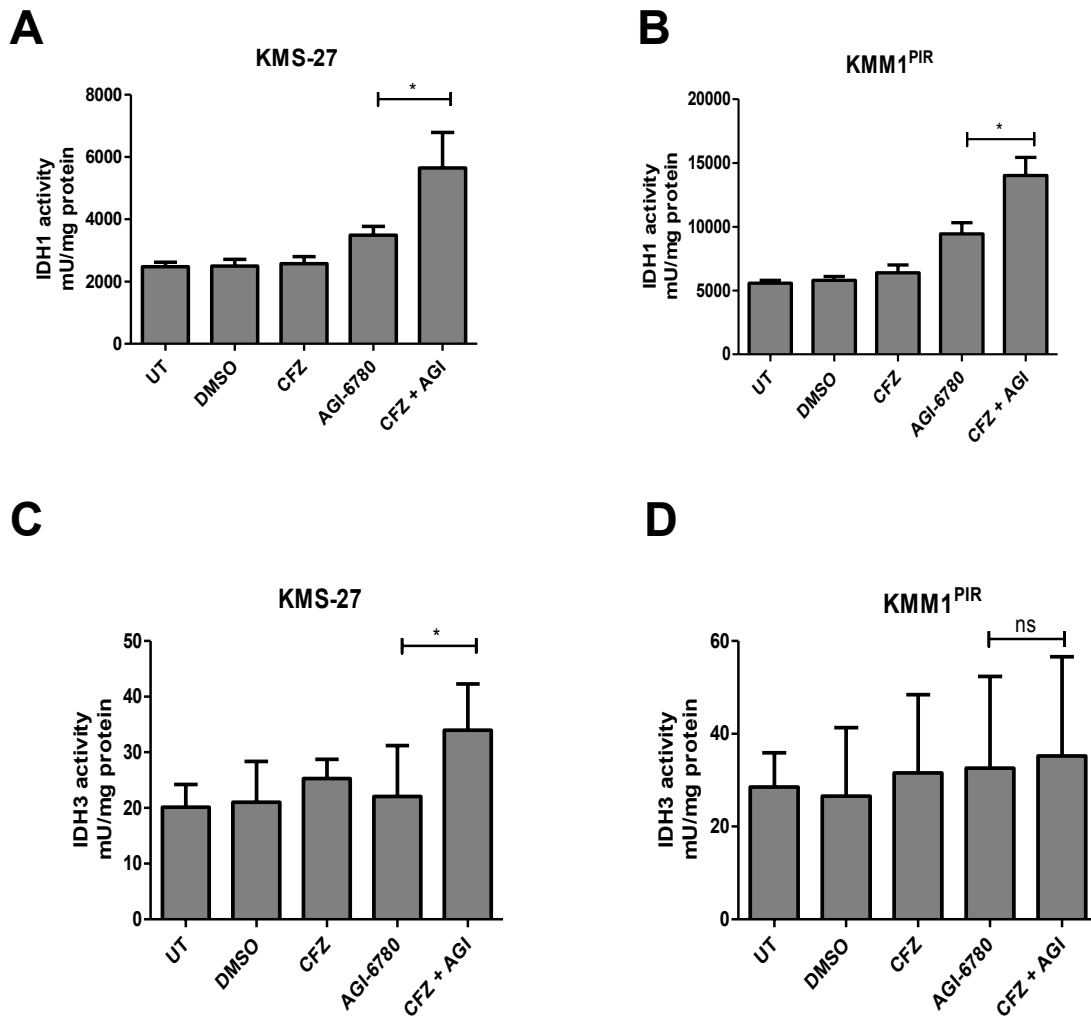


Figure S12. (A-D) KMS-27 and KMM-1^{PIR} untreated (UT), treated with DMSO, CFZ (2.5 nM and 5 nM, respectively), AGI-6780 (5 μM), or the combination of the two drugs were analyzed for (A-B) IDH1 and (C-D) IDH3 activities 6 hours post-treatment. Data are the means ± s.d. of four independent experiments (**P*<0.05).

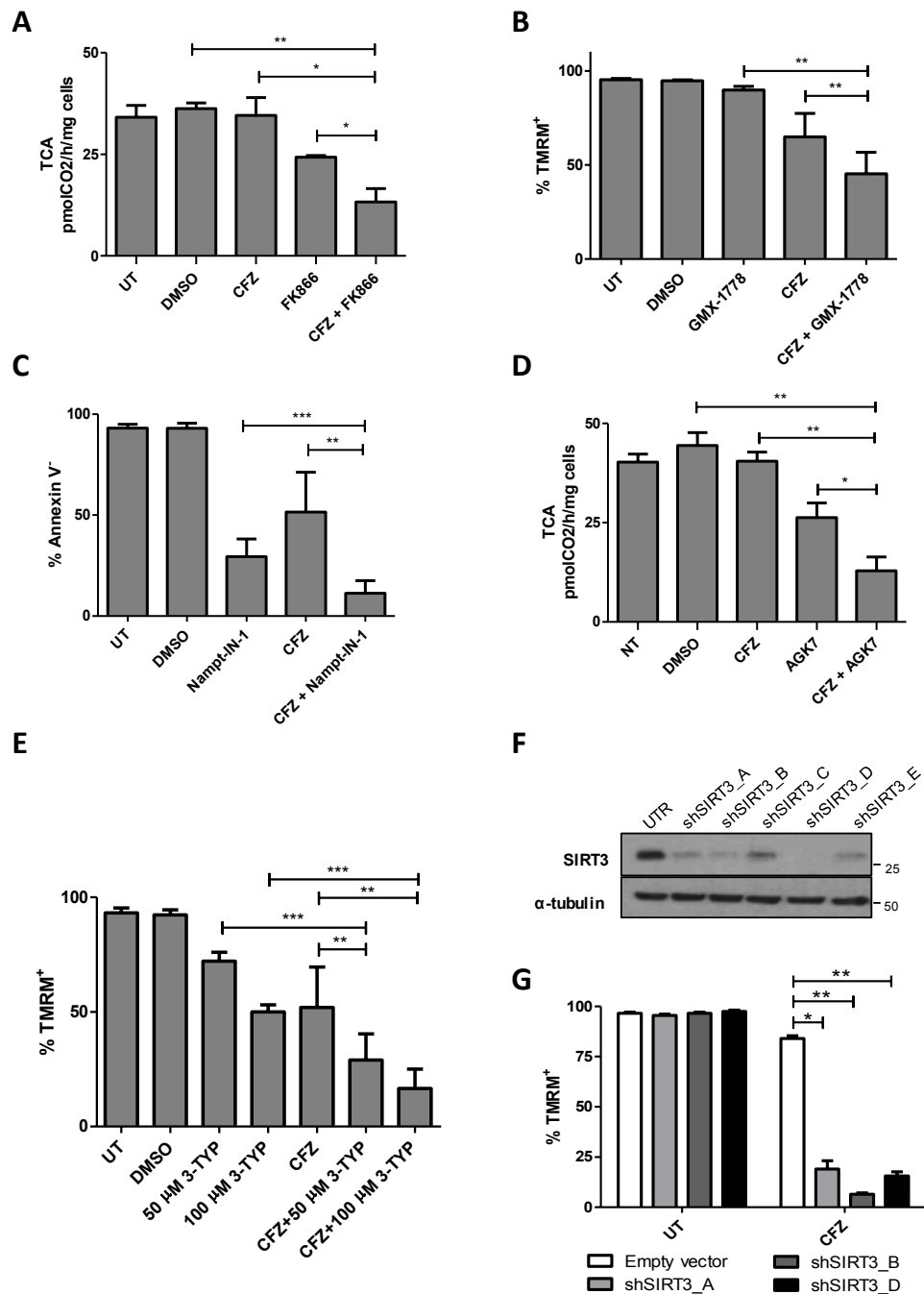


Figure S13. Combinatorial treatment with CFZ and AGI-6780 acts through the inhibition of the NAMPT/SIRT3/IDH2 pathway. (A) KMS-27 cells were left untreated (UT), treated with DMSO, or FK866 (10 nM), for 48 hours, and then vehicle or CFZ (2.5 nM) were added for a further 48 hours. Cells were analyzed for tricarboxylic acid (TCA) cycle activity 6 hours post-treatment with CFZ. Data are the means \pm s.d. of three independent experiments. (B) KMS-27 cells were left untreated (UT), treated with DMSO, or GMX-1778 (10 nM), for 48 hours, and then vehicle or CFZ (2.5 nM) were added for a further 48 hours. Cell viability was measured by TMRM staining-flow cytometry 48 hours post-treatment of CFZ. Data are the means \pm s.d. of three independent experiments. (C) KMS-27 cells were left untreated (UT), treated with DMSO, or Nampt-IN-1 (200 nM), for 48

hours, and then vehicle or CFZ (3.75 nM) were added for a further 48 hours. Cell viability was measured by Annexin⁻ staining-flow cytometry 48 hours post-treatment of CFZ. Data are the means \pm s.d. of five independent experiments. **(D)** KMS-27 cells treated with DMSO, CFZ (1.67 nM), AGK7 (10 μ M), or the combination of the two drugs were analyzed for tricarboxylic acid (TCA) cycle activity 6 hours post-treatment. Data are the means \pm s.d. of three independent experiments. **(E)** KMS-27 cells were left untreated (UT), treated with DMSO, or 3-TYP (50 or 100 μ M), for 48 hours, and then vehicle or CFZ (3.75 nM) were added for a further 48 hours. Cell viability was measured by TMRM staining-flow cytometry 48 hours post-treatment of CFZ. Data are the means \pm s.d. of five independent experiments. **(F)** Representative western blot showing SIRT3 expression levels in KMM-1 cells transduced with lentiviral particles expressing the shRNAs targeting SIRT3 (UTR = untransduced). α -tubulin protein expression was included for protein loading normalization. **(G)** KMM-1 cells were transduced with shRNAs targeting SIRT3 (shSIRT3_A, shSIRT3_B, shSIRT3_D, UTR = untransduced) and treated or not with CFZ (5 nM). Cell viability was measured by TMRM staining-flow cytometry 48 hours post-treatment. Data are the means \pm s.d. of two independent experiments (* P <.05; ** P <.01; *** P <.001).

SUPPLEMENTAL TABLE LEGENDS

Supplemental Table S1. List of target genes used in shRNA screening.

Supplemental Table S2. List of shRNA sequences.

Supplemental Table S3. List of RT-qPCR primers specific for the indicated target sequences.

Supplemental Table S4. Transduction value (T) for each shRNA sequence.

Supplemental Table S5. Growth Rate data.

Supplemental Table S6. Average Z-Scores.

Supplemental Table S7. List of TOP24 genes.

Table S1

ABL1	DNMT2	JAK3	RAC1
ABL2	DNMT3	JNK1	RAC2
AKT1	E2F1	JNK2	RAC3
AKT2	EGFR	JNK3	REL
ALK	EIF4B	JUN	RELA
ARNT1	EIF4E	KDM1A	RELB
ATF1	ENOA	KIT	RHO
ATF3	EP2	KRAS	ROS1
ATG5	EPAS1	LDHA	RPS6
ATG7	ERBB2	LEF1	RUNX1
AURKA	ERBB3	LTA4H	RUNX2
AURKB	ERBB4	LTB4R	SGK1
BATF3	ERK1	LTC4S	SIRT1
BCAR1	ERK2	MAFF	SKP2
BCL2	ETS1	MAML2	SLC2A1
BCL2A1	EZH2	MCL1	SMAD2
BCL3	FBX05	MDM2	SMAD3
BECN1	FLI1	MET	SMAD4
BRAF	FLT3	MLL1	SMO
BTRCP	FOS	MLL2	SNAI2
CA9	GLI1	MTOR	SOX2
CBFB	GLI2	MYC	SRC
CCND1	HDAC1	NANOG	SRCIN1
CDC2	HDAC2	NFKB1	STAT1
CDC42	HDAC6	NFKB2	STAT3
CDH2	HIF1A	NOTCH1	STAT5A
CDK2	HRAS	NOTCH3	STAT5B
CDK4	IAP1	NRAS	TCF4
CDK6	IAP2	OCT4	TERT
CDK7	IDH1	P38	TNS4
CDKN1A	IDH2	PARP1	TRAF6
CEBPB	IGF1R	PDGFRA	TWIST1
CFLIP	IKKA	PDGFRB	UBE2D2
CRAF	IKKB	PGC1A	VEGFR1
CREB	IL17RA	PI3KCA	VEGFR2
CTNNB1	IL23R	PLK1	VEGFR3
CYSLTR1	IRF4	PTGES	XIAP
DNMT1	JAK2	PTK2	ZEB1

Table S2

Table with columns: GENE_SYMBOL, GENE_DESCRIPTION, GENE_ID, REFSEQ_ID, TRC_ID, OLG_SEQ, CLONE_NAME, PLATE_Number, PLATE_ROW, PLATE_COLUMN. The table lists various genes and their corresponding identifiers and sequences.

Table S3

GENE_SYMBOL	Reference_ID_gene_description	Primer_F	Primer_R
ABL1	>NM_005157.4 Homo sapiens c-abl oncogene 1, non-receptor tyrosine kinase (ABL1), transcript variant a, mRNA	GAGCCTGGCCTACAACAAGT	CCTGGACAGGTCAAITCCC
ABL2	>NM_005158.4 Homo sapiens v-abl Abelson murine leukemia viral oncogene homolog 2 (ABL2), transcript variant c, mRNA	AGGTACGAGGGACGTGTGTA	TGGTGTACAAGCTCTGCCAA
AKT1	>NM_005163.2 Homo sapiens v-akt murine thymoma viral oncogene homolog 1 (AKT1), transcript variant 1, mRNA	GCTTCTTGGCCGTATCGTG	GGCCGTGAACCTCCTCATCAA
AKT2	>NM_001626.4 Homo sapiens v-akt murine thymoma viral oncogene homolog 2 (AKT2), transcript variant 1, mRNA	TTTACGCCCACTCCATCAC	CTGGTCCAGCTCCAGTAAGC
ALK	>NM_004304.4 Homo sapiens ALK receptor tyrosine kinase (ALK), transcript variant 1, mRNA	AAGGAGGTGCCCGCGAAAAACA	GCATTCCGACACCTGGCCTTC
ARNT	>NM_001668.3 Homo sapiens aryl hydrocarbon receptor nuclear translocator (ARNT), transcript variant 1, mRNA	ACTTGGACCCCTACTACCCG	GAGCTTAGCAGTAGCTGGG
ATF1	>NM_005171.4 Homo sapiens activating transcription factor 1 (ATF1), mRNA	CGACAGCATAGGCTCTCTAC	CTCCTTTTCTGCCCGTGTA
ATF3	>NM_001674.3 Homo sapiens activating transcription factor 3 (ATF3), transcript variant 1, mRNA	CTGCAAAAGTCGCAAAACAAGA	CACITTCACGCTCTCCGACT
ATG5	>NM_004849.2 Homo sapiens autophagy related 5 (ATG5), mRNA	TCACAAGCAACTCTGGATGGG	GAGTTCCGATTGATGGCCC
ATG7	>NM_006395.2 Homo sapiens autophagy related 7 (ATG7), transcript variant 1, mRNA	CCAACCTCTCTGGGCTTGT	GGCTGACGGGAAGGACATTAT
AURKA	>NM_003600.2 Homo sapiens aurora kinase A (AURKA), transcript variant 2, mRNA	GAGGCATCATGGACCGTCT	TGCTGAGTACGAGAACACCG
AURKB	>NM_004217.3 Homo sapiens aurora kinase B (AURKB), transcript variant 1, mRNA	TGAAGATTGCTGACTTCGGCT	CATCTCTGGGGCAGGTAGT
BATF3	>NM_018664.2 Homo sapiens basic leucine zipper transcription factor, ATF-like 3 (BATF3), mRNA	AGTTGCTGCTCAGAGAAGTCG	TGTTTCTTCTCCAGCTCT
BCAR1	>NM_014567.4 Homo sapiens BCAR1, Cas family scaffold protein (BCAR1), transcript variant 6, mRNA	GGGCAGCTGGTGTGC	GGACTCGGCACATTGTCTAT
BCL2	>NM_000633.2 Homo sapiens B-cell CLL/lymphoma 2 (BCL2), nuclear gene encoding mitochondrial protein, transcript variant alpha, mRNA	ATGTGTGTGGAGAGCGTCAA	GGGCCGTACAGTTCACAAA
BCL2A1	>NM_004049.3 Homo sapiens BCL2-related protein A1 (BCL2A1), transcript variant 1, mRNA	GGATAAGGCAAAACGGAGGC	AGTCATCCAGCCAGATTAGGT
BCL3	>NM_005178.4 Homo sapiens B-cell CLL/lymphoma 3 (BCL3), mRNA	ATGGAACACCCCTCTTCTGC	CCCTGCACACAGCAATATG
BECN1	>NM_003766.3 Homo sapiens beclin 1, autophagy related (BECN1), mRNA	CCCTGAAACTGGACACGAG	TCCTGGTCTCTCTGGTIT
BIRC2	>NM_001166.4 Homo sapiens baculoviral IAP repeat containing 2 (BIRC2), transcript variant 1, mRNA	GGAGAAGAAAATGCTGACCCAC	AAAGCCATTTCGAAGGCAGA
BIRC3	>NM_001165.4 Homo sapiens baculoviral IAP repeat containing 3 (BIRC3), transcript variant 1, mRNA	TGTGATGGTGGACTCAGGTG	TGGCTTGAAGTTCAGCGATGA
BRAF	>NM_004333.4 Homo sapiens v-raf murine sarcoma viral oncogene homolog B1 (BRAF), mRNA	AGGACCTCAGCGAAGGAA	ACTCGAGTCCGCTACCAA
BTRC	>NM_003939.4 Homo sapiens beta-transducin repeat containing E3 ubiquitin protein ligase (BTRC), transcript variant 2, mRNA	GTGAGTGGGCGCTATGTTGG	CTCTCCGGAATGCTCCACA
CA9	>NM_001216.2 Homo sapiens carbonic anhydrase IX (CA9), mRNA	GCCTTGGCCAGAGTTGACGA	CTCTCAAGCGAGACAGCAA
CBFB	>NM_001755.2 Homo sapiens core-binding factor, beta subunit (CBFB), transcript variant 2, mRNA	TGGTATGGGCTGTCTGGAGT	ACCTCATTCTCCCGATG
CCND1	>NM_005306.2 Homo sapiens cyclin D1 (CCND1), mRNA	AGCGGGAGGAGAACAACAG	CATGGAGGGCGGATTGGAAA
CDC42	>NM_001791.3 Homo sapiens cell division cycle 42 (CDC42), transcript variant 1, mRNA	GCAGTACAGTTATGTTGGTG	TGTGGATAACTCAGCGTGG
CDH2	>NM_001792.3 Homo sapiens cadherin 2, type 1, N-cadherin (neuronal) (CDH2), mRNA	TGTGGGAATCCGACGAATGG	CATATGGTGGAGCTGTGGGG
CDK1	>NM_001786.4 Homo sapiens cyclin-dependent kinase 1 (CDK1), transcript variant 1, mRNA	ACCATACCCATTGACTAATGGA	TGGCTACACTTGACTGTAG
CDK2	>NM_001798.3 Homo sapiens cyclin-dependent kinase 2 (CDK2), transcript variant 1, mRNA	CCTGAAATCTCTGGGCTG	CCCAGAGTCCGAAGATCCG
CDK4	>NM_000075.3 Homo sapiens cyclin-dependent kinase 4 (CDK4), mRNA	CCGTGGTGTTCACACTCTGGT	GTCCGGCTCAGAGTTTCCAC
CDK6	>NM_001259.6 Homo sapiens cyclin-dependent kinase 6 (CDK6), transcript variant 1, mRNA	TGACCGCAGCGGACAAAATA	CAAGACTCGGTGCTCTGT
CDK7	>NM_001799.3 Homo sapiens cyclin-dependent kinase 7 (CDK7), mRNA	GTGCAGCAGGAGGACACTTA	AGCTGACATCCAGGTGTTGG
CDKN1A	>NM_000389.4 Homo sapiens cyclin-dependent kinase inhibitor 1A (p21, Cip1) (CDKN1A), transcript variant 1, mRNA	ACTCTCAGGCTCGAAAACCG	GGCGATTAGGGTCTCTCT
CEBPB	>NM_005194.3 Homo sapiens CCAAT/enhancer binding protein (C/EBP), beta (CEBPB), mRNA	CGTTCATGCAACGCTGG	AAGCAGTCCGCCTCGTAGTA
CFLAR	>NM_003879.5 Homo sapiens CASP8 and FADD-like apoptosis regulator (CFLAR), transcript variant 1, mRNA	AATCTGGTTCGCCAGATCAA	ACTTTCCTGCTCTCTGAA
CHUK	>NM_001278.3 Homo sapiens conserved helix-loop-helix ubiquitous kinase (CHUK), mRNA	CCCCGACTCAGCAGAACAT	GTGCTAAATGGCCAAGGCA
CREB1	>NM_004379.3 Homo sapiens cAMP responsive element binding protein 1 (CREB1), transcript variant A, mRNA	GCACAGCACCATGATGGACA	GGGCAATAGTGTACTGGGG
CTNNB1	>NM_001904.3 Homo sapiens catenin (cadherin-associated protein), beta 1, 88kDa (CTNNB1), transcript variant 1, mRNA	CGTGACATCAGGATACCCA	GGCTCCGGTACAACCTCAA
CYSLTR1	>NM_006639.3 Homo sapiens cysteinyl leukotriene receptor 1 (CYSLTR1), transcript variant 3, mRNA	CAGGCTGGGCTTCTCTAAT	CTCTACGAATGCTGCTTGTG
DNMT1	>NM_001379.2 Homo sapiens DNA (cytosine-5)-methyltransferase 1 (DNMT1), transcript variant 2, mRNA	GGCGGCTCAAAGATTTGGAA	TGGTTTCAAAGTCACATACTGAT
DNMT3A	>NM_002252.4 Homo sapiens DNA methyltransferase 3 alpha (DNMT3A), transcript variant 3, mRNA	GAGAGCAGAGGACGAGCC	CTGTGAGCTGTGGGTGG
DNMT3B	>NM_006892.3 Homo sapiens DNA (cytosine-5)-methyltransferase 3 beta (DNMT3B), transcript variant 1, mRNA	ACCAGTGGTTAATAGTCGAAGG	CAGTAGTCAGAGGTGGCTGA
E2F1	>NM_005225.2 Homo sapiens E2F transcription factor 1 (E2F1), mRNA	GCCAAGAAGTCCAAGAACACA	TCAACCCCTCAAGCCGTC
EGFR	>NM_005228.4 Homo sapiens epidermal growth factor receptor (EGFR), transcript variant 1, mRNA	CTCCTGGCGCTGCTGG	TGCGTGAAGCTTGTACTCT
EIF4B	>NM_001417.4 Homo sapiens eukaryotic translation initiation factor 4B (EIF4B), mRNA	GTACTGGTGGAGGAAGCACC	GGAGGCGCCTATACACATC
EIF4E	>NM_001968.3 Homo sapiens eukaryotic translation initiation factor 4E (EIF4E), transcript variant 1, mRNA	TGATGTATGGCGCTGTTG	TGGAGGAAGTCTCAACCTTCC
EPAS1	>NM_001430.4 Homo sapiens endothelial PAS domain protein 1 (EPAS1), mRNA	GGCACCATGAGGAGATTCTG	GACCGTCACTTATCTCTCA
ERBB2	>NM_004448.2 Homo sapiens v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian) (ERBB2), transcript variant 1, mRNA	CCGAGGGCCGGTATACCTTC	TGCTGTCACTTCTGGTGTG
ERBB3	>NM_001982.3 Homo sapiens v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian) (ERBB3), transcript variant 1, mRNA	TGAGATTGTGCTGACGGAC	GGAGGTTGGGCAATGGTAGA
ERBB4	>NM_005235.2 Homo sapiens erb-b2 receptor tyrosine kinase 4 (ERBB4), transcript variant JM-a/CVT-1, mRNA	ACGGGCCATTCCACTTACC	ACCAGAATGAAGGCCACCC
ERK1	>NM_002746.2 Homo sapiens mitogen-activated protein kinase 3 (MAPK3), transcript variant 1, mRNA	TCATCGGCATCCGAGACATT	CTCAGCTGCTGGTITTCAG
ERK2	>NM_002745.4 Homo sapiens mitogen-activated protein kinase 1 (MAPK1), transcript variant 1, mRNA	CGCTACCAACCTCTCGTA	GGTGTCAAAGGGGCTGATT
ETS1	>NM_005238.3 Homo sapiens v-ets erythroblastosis virus E26 oncogene homolog 1 (avian) (ETS1), transcript variant 2, mRNA	AACATGTGCATGGGGAGGAC	CTGGGTGAGGCGATCACAC
EZH2	>NM_004456.4 Homo sapiens enhancer of zeste homolog 2 (Drosophila) (EZH2), transcript variant 1, mRNA	ACGCTTTTCTGTAGCGGATGT	AAGTGTGGGTGTTGCATTGA
FBXO5	>NM_012177.3 Homo sapiens F-box protein 5 (FBXO5), transcript variant 1, mRNA	GCCTCGACCTCGGATA	AGTTTAAAGTCCGGAATGAACATGG
FLI1	>NM_002017.4 Homo sapiens Friend leukemia virus integration 1 (FLI1), transcript variant 1, mRNA	AATACAGAGCAAGCGCCC	AGAGCAGCTCCAGGAGGAAT
FLT1	>NM_002019.4 Homo sapiens fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1), transcript variant 1, mRNA	CAAATAAGCACACCAGCCC	CGCCTACGGAAGCTCTCT
FLT3	>NM_004119.2 Homo sapiens fms-related tyrosine kinase 3 (FLT3), mRNA	GTGCTTTGCGATTACAGGG	GCACCTTATGTCGGTCCAA
FLT4	>NM_002020.4 Homo sapiens fms-related tyrosine kinase 4 (FLT4), transcript variant 2, mRNA	AGATGTTTGGCCAGCTAGT	TTCCCTCCACAACTCGGTC
FOS	>NM_005252.3 Homo sapiens Fos proto-oncogene, AP-1 transcription factor subunit (FOS), mRNA	GGAGAATCCGAAGGAAAAGGA	AGTTGGTCTGTCCGCTTG
GLI1	>NM_005269.2 Homo sapiens GLI family zinc finger 1 (GLI1), transcript variant 1, mRNA	CCCTGGACCGCATC	CGAGTTGAACATGGCGTCTC
GLI2	>NM_005270.4 Homo sapiens GLI family zinc finger 2 (GLI2), mRNA	AAAGCCTCTCTTGGTGG	TCGCATGCAATCGGTAGGG
HDAC1	>NM_004964.2 Homo sapiens histone deacetylase 1 (HDAC1), mRNA	ACGGGATTGATGACGAGTCC	CACACTGTAAAGCACCCGCA
HDAC2	>NM_001527.3 Homo sapiens histone deacetylase 2 (HDAC2), transcript variant 1, mRNA	ATGGCGTACAGTCAAGGAGG	CATGGGATGACCTGTCCA
HDAC6	>NM_006044.3 Homo sapiens histone deacetylase 6 (HDAC6), transcript variant 5, mRNA	CCACGGTCAAGGAACACAGT	GTGGTGGACAGTTAGAGGC
HIF1A	>NM_001530.3 Homo sapiens hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) (HIF1A), transcript variant 1, mRNA	TCCAAGAAGCCCTAACGTTG	CGCTTCTCTGAGCATTCTGC

Table S3

GENE SYMBOL	Reference ID, gene description	Primer F	Primer R
HRAS	>NM_005343.3 Homo sapiens HRAS proto-oncogene, GTPase (HRAS), transcript variant 1, mRNA	CTACACGTTGGTGCGTGAGA	CTGTGCTGCGTCAGGAGAG
IDH1	>NM_005896.3 Homo sapiens isocitrate dehydrogenase (NADP+) 1, cytosolic (IDH1), transcript variant 1, mRNA	CAAGACTGGGAGAACTGGG	TGCATCTACCACAGAACCC
IDH2	>NM_002168.2 Homo sapiens isocitrate dehydrogenase 2 (NADP+), mitochondrial (IDH2), nuclear gene encoding mitochondrial protein, mRNA	CGGAGATGTGACGTACAGA	GCCTCAGCTCAATCGTCT
IGF1R	>NM_000875.3 Homo sapiens insulin-like growth factor 1 receptor (IGF1R), mRNA	TCTCTCTGGGAATGGGTGCT	CAACCCCTCCACGATCAACA
IKBK	>NM_001556.2 Homo sapiens inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta (IKBK), transcript variant 1, mRNA	TGAGAAGACTGTGTTCCGGC	AGGCATTCATGCTATCCGGG
IL17RA	>NM_014339.6 Homo sapiens interleukin 17 receptor A (IL17RA), transcript variant 1, mRNA	CTGTCTCTGCTGCTCCG	TTTGACCGTGCACTTTAGCC
IL23R	>NM_144701.2 Homo sapiens interleukin 23 receptor (IL23R), mRNA	CCTGGCTCTGAAGTGGAAATTA	AAGGGCTATTACTGCATCCC
IRF4	>NM_002460.3 Homo sapiens interferon regulatory factor 4 (IRF4), transcript variant 1, mRNA	GGCAAGCAGGACTACAACCG	TTGTGATGCCTCTCGGAAC
JAK2	>NM_004972.3 Homo sapiens Janus kinase 2 (JAK2), mRNA	TGGGAGCAACAGAGCCTATC	TCCGTGCACAAATCATGCC
JAK3	>NM_000215.3 Homo sapiens Janus kinase 3 (JAK3), mRNA	GAGTGGGACTTTCCTCTCCG	ACTTGGAGGTGCCATGAGTG
JUN	>NM_002228.3 Homo sapiens jun proto-oncogene (JUN), mRNA	CTTTTCAAAGCCGGTAGCG	TTTCTCTAAGAGCGCACGA
KDM1A	>NM_015013.3 Homo sapiens lysine demethylase 1A (KDM1A), transcript variant 2, mRNA	AGCCATGGTGGTAAACAGGTC	AGCTTCTCCGTGGCTTCATA
KDR	>NM_002253.2 Homo sapiens kinase insert domain receptor (a type III receptor tyrosine kinase) (KDR), mRNA	GTACACCTGTGCAGATCCA	CCACCAGAGATTCATGCCA
KIT	>NM_000222.2 Homo sapiens v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog (KIT), transcript variant 1, mRNA	GGCAGGTTGAATGAAGGC	CAGGTTGTGGGATGGAATT
KRAS	>NM_004985.3 Homo sapiens v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), transcript variant b, mRNA	TAGGCAAGAGTGCTTGAGC	CCAAGAGACAGTTTCTCCATCA
KRAS	>NM_033360.3 Homo sapiens KRAS proto-oncogene, GTPase (KRAS), transcript variant a, mRNA	GACTCCTGGCTGTGTGAAA	GTATAGAAGGCATCATCAACACC
LDHA	>NM_005566.3 Homo sapiens lactate dehydrogenase A (LDHA), transcript variant 1, mRNA	GCCGATTCGGGATCTCATTG	CAGCTGATCCTTTAGAGTTGCC
LEF1	>NM_016269.4 Homo sapiens lymphoid enhancer-binding factor 1 (LEF1), transcript variant 1, mRNA	CCGAAAGGAGGAAGCGATTTA	AGGGCTCTGAGAGGTTTGT
LTA4H	>NM_000895.2 Homo sapiens leukotriene A4 hydrolase (LTA4H), transcript variant 1, mRNA	GGCGACAAGTCACTTCCAA	GCAATGTGGCGTCCAAGT
LTBR	>NM_181657.3 Homo sapiens leukotriene B4 receptor (LTBR), transcript variant 1, mRNA	CCCTGGAGTTTCTGTCCCA	CGGATGTGAGAGAAATGGCAA
LTC4S	>NM_000897.2 Homo sapiens leukotriene C4 synthase (LTC4S), transcript variant 2, mRNA	GTCCGACGACCATCCCC	GGGAAGTACTCGCTGCAGTT
MAFF	>NM_012323.3 Homo sapiens v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F (MAFF), transcript variant 1, mRNA	GAGGGCAGCTCTGCAAAACAT	TTCTCGCTCAGCTCTCGCTT
MAML2	>NM_032427.3 Homo sapiens mastermind like transcriptional coactivator 2 (MAML2), mRNA	AGGGGACCGAGGAACTCAG	CATTGGGTGCTGTGCTGTG
MAPK14	>NM_001315.2 Homo sapiens mitogen-activated protein kinase 14 (MAPK14), transcript variant 1, mRNA	AGAACCTACAGAGAAGTGGG	TCAGATCTGCCCCATGAGA
MAPK8	>NM_139049.3 Homo sapiens mitogen-activated protein kinase 8 (MAPK8), transcript variant JNK1-a2, mRNA	CTCGCTACTACAGAGCACCC	CTCCATAATGACCCCCACA
MAPK9	>NM_002752.4 Homo sapiens mitogen-activated protein kinase 9 (MAPK9), transcript variant JNK2-a2, mRNA	TTACTGTGTGACACGGTACT	GATGCAACCACTGACAGACA
MCL1	>NM_021960.4 Homo sapiens MCL1, BCL2 family apoptosis regulator (MCL1), transcript variant 1, mRNA	AAGGACAAAAGGGACTGGC	GCAAAAGCCAGCAGACAT
MDM2	>NM_002392.4 Homo sapiens Mdm2, p53 E3 ubiquitin protein ligase homolog (mouse) (MDM2), mRNA	AGGAGATTTGTTGGCGTGC	TGAGTCCGATGTTCTGCTG
MET	>NM_000245.2 Homo sapiens met proto-oncogene (hepatocyte growth factor receptor) (MET), transcript variant 2, mRNA	CCGAAAGTGAAGCCCAACT	AGGATACTGCACTGTCGGC
MLL	>NM_005933.3 Homo sapiens lysine methyltransferase 2A (KMT2A), transcript variant 2, mRNA	CTGTCAAGTTTGTGGAAGCG	TGGGGGTAGTTTGTGCCAG
MLL2	>NM_003482.3 Homo sapiens myeloid/lymphoid or mixed-lineage leukemia 2 (MLL2), mRNA	GCCTACGTGGTAAAGCGCTG	CAAGGCGATGCCAGTTTCTG
MTOR	>NM_004958.3 Homo sapiens mechanistic target of rapamycin (serine/threonine kinase) (MTOR), mRNA	GACGAGAGATCATCCGCCAG	ACAAGGGACCCACCAATAAG
MYC	>NM_002467.4 Homo sapiens v-myc myelocytomatosis viral oncogene homolog (avian) (MYC), mRNA	GGACCCGCTCTCTGAAGG	TAACGTTGAGGGGCTGCTC
NANOG	>NM_024865.2 Homo sapiens Nanog homeobox (NANOG), mRNA	CTATGCCGTGTGTTTGTGGCG	AGCAGATCCATGAGGAGAGG
NFKB1	>NM_003998.3 Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (NFKB1), transcript variant 1, mRNA	CTGGACCAAGGACATGGTG	GCCTTATACACGCTCTG
NFKB2	>NM_002502.4 Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100) (NFKB2), transcript variant 2, mRNA	CTGTCTGACATGGGCTAGA	CGCACTGCTTCTTCTGCTG
NOTCH1	>NM_017617.5 Homo sapiens notch 1 (NOTCH1), mRNA	TACAAGTCCAAGTCTGCTG	ATAGTCTCGGATGGCTGC
NOTCH3	>NM_000435.2 Homo sapiens notch 3 (NOTCH3), mRNA	TTTGAGTCTGCGTGTAGCT	TCTCCAGTTACAAAGGGC
NRAS	>NM_002524.4 Homo sapiens neuroblastoma RAS viral (v-ras) oncogene homolog (NRAS), mRNA	GGGAAAAGCGCACTGCAAT	TCTCAACAAACAGGTTTACCA
PARP1	>NM_001618.3 Homo sapiens poly (ADP-ribose) polymerase 1 (PARP1), mRNA	GAAGTACGTGCAAGGGGTG	CAACGGTCAATCATGCTCA
PDGFRA	>NM_033023.4 Homo sapiens platelet-derived growth factor alpha polypeptide (PDGFA), transcript variant 2, mRNA	GGGTCCATGCCAATAGCAT	AATGACCTCTGGTCTGC
PDGFRB	>NM_002609.3 Homo sapiens platelet-derived growth factor receptor, beta polypeptide (PDGFRB), mRNA	CATGAGGATGCTGAGTCCAG	TTAGTCCAGCACTCGGACA
PIK3CA	>NM_006218.3 Homo sapiens phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), mRNA	TAGGCAAGTGGAGCAATGG	CTGGTCCGCTATTGCTCA
PLK1	>NM_005030.3 Homo sapiens polo-like kinase 1 (PLK1), mRNA >gi 33876611 gb BC002369.2 Homo sapiens polo-like kinase 1 (Drosophila), mRNA (cDNA clone MGC:8502 IMAGE:2822226), complete cds	AAAGGGCACAGTTTCGAGGT	AGGTGGTTTGCCCAATAACA
POU5F1B	>NM_001159542.1 Homo sapiens POU class 5 homeobox 1B (POU5F1B), mRNA >gi 94490331 gb DQ486513.1 Homo sapiens POU domain transcription factor Oct-4 (POU5F1) mRNA	TGATGCTCAGGCACTGTGT	GGCTGGTGAATGAGCAAT
PPARGC1A	>NM_013261.4 Homo sapiens PPARG coactivator 1 alpha (PPARGC1A), transcript variant 2, mRNA	ACTGGCGTCACTCAGGAGCTG	TCTTCAACCAACAGAGCAGCA
PTGER2	>NM_000956.3 Homo sapiens prostaglandin E receptor 2 (subtype EP2), 53kDa (PTGER2), mRNA	ACCACCTCATCTCCTGGCTA	AAGAGCTTGGAGTCCCAATT
PTGES	>NM_004878.4 Homo sapiens prostaglandin E synthase (PTGES), mRNA	AGAAGGCCTTGGCAACCC	AGATGGTCTCCATGCTGTTCC
PTK2	>NM_005607.4 Homo sapiens protein tyrosine kinase 2 (PTK2), transcript variant 2, mRNA	CAACCACCTGGCCAGTATT	ACGAGCCACATGCTTCCCA
RAC1	>NM_006908.4 Homo sapiens ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1) (RAC1), transcript variant Rac1, mRNA	TGATGACAGGCATCAAGTGT	CCAGGAAATGATTGGTTGTGT
RAC2	>NM_002872.3 Homo sapiens ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2) (RAC2), mRNA	GTCAACCCAGACACTCTG	TGTAGCTGATGAGAAGGACGG
RAC3	>NM_005052.2 Homo sapiens ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3) (RAC3), mRNA	CGGCTCTTGGAGAATGTT	CAATGTGTCTTCTGCTGC
RAF1	>NM_002880.3 Homo sapiens v-raf-1 murine leukemia viral oncogene homolog 1 (RAF1), mRNA	AACGACAGACGTTGGGGC	CAAAGTCCCTGTATGTGTC
REL	>NM_002908.2 Homo sapiens v-rel reticuloendotheliosis viral oncogene homolog (avian) (REL), mRNA	CCTGGTCTCCTGGTCAAT	TGACTTGAACCCCTGATGGC
RELA	>NM_021975.3 Homo sapiens RELA proto-oncogene, NF-kB subunit (RELA), transcript variant 1, mRNA	GGATGGCTCTATGAGCGCTG	TCTGGATGCGCTGACTCA
RELB	>NM_006509.3 Homo sapiens RELB proto-oncogene, NF-kB subunit (RELB), mRNA	GACCTCTCCTCACTCGCT	TGATGTACTGCTGATGATCCC
RHO	>NM_000539.3 Homo sapiens rhodopsin (RHO), mRNA	TTTGAGGGCTCTTTGCCA	TTACACACCACAGTACCG
ROS1	>NM_002944.2 Homo sapiens c-ros oncogene 1, receptor tyrosine kinase (ROS1), mRNA	TTGACCTTGGCACACACAT	TACAGCAACCTCACAGCAG
RPS6	>NM_001010.2 Homo sapiens ribosomal protein S6 (RPS6), mRNA	GCCCCAAAAGAGCTGACAGA	ACGCTGAATCTGGGTCTT
RUNX1	>NM_001754.4 Homo sapiens runt-related transcription factor 1 (RUNX1), transcript variant 1, mRNA	CCTCAGGTTTGGCGTCGAA	CTTGGGTTGGTTTGTGAAG
RUNX2	>NM_004348.3 Homo sapiens runt-related transcription factor 2 (RUNX2), transcript variant 3, mRNA	CCCTGAACCTGCAACCAAT	GGCTCAGGTAGGAGGGTAA
SGK	>NM_005627.3 Homo sapiens serum/glucocorticoid regulated kinase 1 (SGK1), transcript variant 1, mRNA	CTCGGGCCAAAGGATGACT	GCCCACTCACATTTGGGTTAA
SIRT1	>NM_012238.4 Homo sapiens sirtuin 1 (SIRT1), transcript variant 1, mRNA	GGAGCAGATTAGTAGCGGCG	CCTCAGCCGATGGAAAATG
SKP2	>NM_005983.3 Homo sapiens S-phase kinase associated protein 2 (SKP2), transcript variant 1, mRNA	GCTGCTAAAGTCTCTGGTGT	AGCAACCCAGCAGTCAATC
SLC2A1	>NM_006516.3 Homo sapiens solute carrier family 2 member 1 (SLC2A1), mRNA	TCCCTGCAGTTTGGCTACAA	CAGGATGCTCTCCCATAGC
SMAD2	>NM_005901.5 Homo sapiens SMAD family member 2 (SMAD2), transcript variant 1, mRNA	AGGAAGGAAACAAAGTCCCG	CTTACCAAGGAGCAAGCC

Table S3

GENE SYMBOL	Reference ID, gene description	Primer F	Primer R
SMAD3	>NM_005902.3 Homo sapiens SMAD family member 3 (SMAD3), transcript variant 1, mRNA	GAAACTCAAGAAGACGGGGCAG	CGATGGGACACCTGCAACC
SMAD4	>NM_005359.5 Homo sapiens SMAD family member 4 (SMAD4), mRNA	ACATTGGATGGGAGGCTTCTCAG	CCTCCAGAGACGGGCATAGA
SMO	>NM_005631.4 Homo sapiens smoothened, frizzled family receptor (SMO), mRNA	TCCTGACCGCTTCCCTGAA	TCTTGGGTTGTCTGTCCGA
SNAI2	>NM_003068.4 Homo sapiens snail homolog 2 (Drosophila) (SNAI2), mRNA	ACGCTCCAAAAGCCAAAC	GGCTGTATGCTCTGAGCTG
SOX2	>NM_003106.3 Homo sapiens SRY (sex determining region Y)-box 2 (SOX2), mRNA	TGCTGCCTCTTAAGACTAGGAC	CGCCCGATGATTGTTATT
SRC	>NM_005417.4 Homo sapiens SRC proto-oncogene, non-receptor tyrosine kinase (SRC), transcript variant 1, mRNA	GCTCAATGCAGAGAACCCGA	GACACTGAGAGGCAGTAGGC
SRCIN1	>NM_025248.2 Homo sapiens SRC kinase signaling inhibitor 1 (SRCIN1), mRNA	CAAGGACGAGGATGACGAGG	TTCATGGGTGGTACACTGCC
STAT1	>NM_007315.3 Homo sapiens signal transducer and activator of transcription 1, 91kDa (STAT1), transcript variant alpha, mRNA	GAGGTGTCTCGGATAGTGGG	TGAGAAGGAAAAGTGCGCC
STAT3	>NM_139276.2 Homo sapiens signal transducer and activator of transcription 3 (STAT3), transcript variant 1, mRNA	CTGCTCAGGTACCGTGTGT	CCTCTGCCGAGAAACAG
STAT5A	>NM_003152.3 Homo sapiens signal transducer and activator of transcription 5A (STAT5A), mRNA	CCCCAGCTCCCTATAACAT	ATCCAGGTGCAATCTCCATCC
STAT5B	>NM_012448.3 Homo sapiens signal transducer and activator of transcription 5B (STAT5B), mRNA	CATTTCCATTGAGGTGCGG	AGGAGCTGGGTGGCCTAAT
TCF4	>NM_003199.2 Homo sapiens transcription factor 4 (TCF4), transcript variant 2, mRNA	TGAGAACCTGCAAGACACGA	GGTGTACAGTCTCATCGTC
TERT	>NM_198253.2 Homo sapiens telomerase reverse transcriptase (TERT), transcript variant 1, mRNA	TACTGCGTGGTGGTATG	ATGTACGGCTGGAGGTCTGT
TERT	>NM_198253.2 Homo sapiens telomerase reverse transcriptase (TERT), transcript variant 1, mRNA	CTCCTGCTTTGTGGATGA	AAGTTCACCGCAGCCATA
TNS4	>NM_032865.5 Homo sapiens tensin 4 (TNS4), mRNA	GGAGCCAGTAGTGAAGGCAA	CCAGCCTACTGACATCCC
TRAF6	>NM_004620.3 Homo sapiens TNF receptor-associated factor 6, E3 ubiquitin protein ligase (TRAF6), transcript variant 2, mRNA	GACCAGAACTGCTTTGGCA	AATGTGCATGGAATTGGGGC
TWIST1	>NM_000474.3 Homo sapiens twist homolog 1 (Drosophila) (TWIST1), mRNA	TTCTCGGCTGAGGATGGA	AATGACATCTAGGCTCCGGC
UBE2D2	>NM_003339.2 Homo sapiens ubiquitin-conjugating enzyme E2D 2 (UBE2D2), transcript variant 1, mRNA	TGAATGATCTGGCACGGGAC	TAGGACTGTCTTTGGCCC
XIAP	>NM_001167.3 Homo sapiens X-linked inhibitor of apoptosis (XIAP), transcript variant 1, mRNA	ACTTGAGGTTCTGTGGCAG	CGCCTTAGCTCTCTCAGTA
ZEB1	>NM_030751.5 Homo sapiens zinc finger E-box binding homeobox 1 (ZEB1), transcript variant 2, mRNA	CAGGTGAAGCGCAGAAAGC	TGAGTTTGTCTTCATCATCTGAAT

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
ABL1	4	G	5	51,89
ABL1	4	G	6	22,50
ABL1	4	G	7	20,58
ABL1	4	G	8	19,20
ABL1	4	G	9	8,08
ABL2	4	G	10	14,04
ABL2	4	G	11	13,82
ABL2	4	G	12	6,84
ABL2	4	H	1	40,69
ABL2	4	H	2	35,42
AKT1	4	H	3	31,27
AKT1	4	H	4	29,53
AKT1	4	H	5	39,63
AKT1	4	H	6	28,04
AKT1	4	H	7	13,78
AKT2	2	C	9	31,01
AKT2	2	C	10	74,43
AKT2	2	C	11	84,74
AKT2	2	C	12	21,72
AKT2	2	D	1	15,74
ALK	8	G	6	35,70
ARNT	2	D	2	24,47
ARNT	2	D	3	26,55
ARNT	2	D	4	53,24
ARNT	2	D	5	75,97
ARNT	2	D	6	42,81
ATF1	4	H	8	10,89
ATF1	4	H	9	13,10
ATF1	4	H	10	11,79
ATF1	4	H	11	8,59
ATF1	4	H	12	4,40
ATF3	8	G	10	35,91
ATF3	8	G	11	2,56
ATG5	4	D	5	47,77
ATG5	4	D	6	34,42
ATG5	4	D	7	20,76
ATG5	4	D	8	6,63
ATG5	4	D	9	5,26
ATG7	5	G	12	8,17
AURKA	8	E	10	4,35
AURKA	8	E	11	4,02
AURKA	8	E	12	5,55
AURKA	8	F	1	2,85
AURKA	8	F	2	2,39
AURKB	4	A	11	3,90
AURKB	4	A	12	5,86
AURKB	4	B	1	11,01
AURKB	4	B	2	24,42

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
AURKB	4	B	3	52,35
BATF3	8	G	7	29,80
BATF3	8	G	8	13,70
BATF3	8	G	9	41,14
BCAR1	6	D	3	75,27
BCAR1	6	D	4	51,58
BCAR1	6	D	5	68,84
BCL2	1	C	12	24,79
BCL2	1	D	1	21,69
BCL2	1	D	2	26,39
BCL2	1	D	3	26,06
BCL2	1	D	4	53,05
BCL2A1	8	G	12	11,64
BCL2A1	8	H	1	10,16
BCL3	8	D	4	8,08
BCL3	8	D	5	44,38
BCL3	8	D	6	25,37
BCL3	8	D	7	50,11
BCL3	8	D	8	8,94
BECN1	3	H	4	12,69
BECN1	3	H	5	14,47
BECN1	3	H	6	31,74
BECN1	3	H	7	15,08
BECN1	3	H	8	4,58
BIRC2	1	G	3	47,44
BIRC2	1	G	4	32,09
BIRC2	1	G	5	53,56
BIRC2	1	G	6	52,76
BIRC2	1	G	7	21,90
BIRC3	1	F	10	38,07
BIRC3	1	F	11	42,99
BIRC3	1	F	12	10,24
BIRC3	1	G	1	22,76
BIRC3	1	G	2	31,73
BRAF	4	B	4	44,91
BRAF	4	B	5	46,02
BRAF	4	B	6	28,81
BRAF	4	B	7	16,16
BRAF	4	B	8	17,36
BTRC	4	A	2	29,57
BTRC	4	A	3	30,73
BTRC	4	A	4	16,75
BTRC	4	A	5	18,51
CA9	1	H	1	21,28
CA9	1	H	2	15,31
CA9	1	H	3	5,39
CA9	1	H	4	12,38
CA9	1	H	5	22,97

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
CBFB	2	D	12	33,85
CBFB	2	E	1	23,37
CBFB	2	E	2	29,86
CBFB	2	E	3	19,02
CBFB	2	E	4	38,77
CCND1	6	H	7	26,91
CCND1	6	H	8	19,77
CCND1	6	H	9	19,52
CCND1	6	H	10	10,96
CCND1	6	H	11	12,97
CDC42	8	A	1	9,44
CDC42	8	A	2	14,07
CDH2	2	E	10	44,42
CDH2	2	E	11	75,82
CDH2	2	E	12	17,64
CDH2	2	F	1	16,35
CDH2	2	F	2	25,26
CDK1	2	E	5	59,12
CDK1	2	E	6	37,82
CDK1	2	E	7	19,42
CDK1	2	E	8	46,97
CDK1	2	E	9	79,91
CDK2	2	F	3	16,50
CDK2	2	F	4	42,73
CDK2	2	F	5	3,80
CDK2	2	F	6	22,06
CDK2	2	F	7	29,55
CDK4	1	A	1	11,76
CDK4	1	A	2	17,93
CDK4	1	A	3	28,37
CDK4	1	A	4	20,94
CDK4	1	A	5	23,29
CDK6	1	H	7	24,07
CDK6	1	H	8	43,79
CDK6	1	H	9	13,15
CDK7	2	F	8	73,42
CDK7	2	F	9	67,77
CDK7	2	F	10	99,96
CDK7	2	F	11	91,64
CDK7	2	F	12	47,77
CDKN1A	8	B	11	24,21
CDKN1A	8	B	12	24,74
CDKN1A	8	C	1	15,85
CEBPB	8	B	1	13,82
CEBPB	8	B	2	23,44
CFLAR	3	H	9	26,97
CFLAR	3	H	10	8,81
CFLAR	3	H	11	9,37

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
CFLAR	3	H	12	11,43
CFLAR	4	A	1	30,00
CHUK	1	H	10	19,07
CHUK	1	H	11	22,63
CHUK	1	H	12	13,74
CHUK	2	A	1	4,01
CHUK	2	A	2	12,93
CREB1	4	B	10	10,36
CREB1	4	B	11	12,05
CREB1	4	B	12	7,16
CREB1	4	C	1	31,41
CREB1	4	C	2	41,33
CTNNB1	2	G	1	34,63
CTNNB1	2	G	2	14,07
CTNNB1	2	G	3	20,36
CTNNB1	2	G	4	42,30
CTNNB1	2	G	5	20,66
CYSLTR1	5	H	11	8,78
CYSLTR1	5	H	12	6,14
CYSLTR1	6	A	1	27,65
CYSLTR1	6	A	2	34,69
CYSLTR1	6	A	3	39,69
DNMT1	2	A	8	12,90
DNMT1	2	A	9	46,03
DNMT1	2	A	10	70,44
DNMT1	2	A	11	81,59
DNMT1	2	A	12	23,75
DNMT3A	6	F	2	57,30
DNMT3A	6	F	3	63,29
DNMT3A	6	F	4	43,71
DNMT3A	6	F	5	57,50
DNMT3A	6	F	6	28,25
DNMT3B	6	A	4	38,56
DNMT3B	6	A	5	19,38
DNMT3B	6	A	6	13,90
DNMT3B	6	A	7	22,07
DNMT3B	6	A	8	19,68
E2F1	5	A	1	21,99
E2F1	5	A	2	22,80
E2F1	5	A	3	30,58
E2F1	5	A	4	24,05
E2F1	5	A	5	19,58
EGFR	5	A	6	15,59
EGFR	5	A	7	13,21
EGFR	5	A	8	12,05
EGFR	5	A	9	12,25
EGFR	5	A	10	12,39
EIF4B	2	B	1	2,85

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
EIF4B	2	B	2	29,92
EIF4B	2	B	3	21,16
EIF4B	2	B	4	53,77
EIF4B	2	B	5	59,83
EIF4E	2	G	6	15,46
EIF4E	2	G	7	31,88
EIF4E	2	G	8	39,68
EIF4E	2	G	9	68,68
EIF4E	2	G	10	79,02
EPAS1	8	G	1	17,30
EPAS1	8	G	2	29,42
EPAS1	8	G	3	12,20
EPAS1	8	G	4	6,43
EPAS1	8	G	5	2,78
ERBB2	4	C	3	26,32
ERBB2	4	C	4	31,20
ERBB2	4	C	5	59,84
ERBB2	4	C	6	21,49
ERBB2	4	C	7	18,45
ERBB3	2	G	11	75,47
ERBB3	2	G	12	58,87
ERBB3	2	H	1	12,17
ERBB3	2	H	2	8,74
ERBB3	2	H	3	17,02
ERBB4	5	A	11	7,24
ERBB4	5	A	12	7,32
ERBB4	5	B	1	19,04
ERBB4	5	B	2	29,11
ERBB4	5	B	3	36,05
ERK1	8	H	2	5,34
ERK2	8	H	3	2,65
ETS1	8	E	2	13,81
ETS1	8	E	3	22,72
EZH2	4	C	8	11,89
EZH2	4	C	9	13,36
EZH2	4	C	10	5,51
EZH2	4	C	11	11,58
FBXO5	6	B	2	36,06
FBXO5	6	B	3	51,18
FBXO5	6	B	4	53,62
FBXO5	6	B	5	19,12
FBXO5	6	B	6	36,61
FLI1	8	E	4	18,35
FLI1	8	E	5	49,08
FLT1	2	H	4	22,57
FLT1	2	H	5	24,96
FLT1	2	H	6	23,04
FLT1	2	H	7	30,69

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
FLT1	2	H	8	24,32
FLT3	4	A	6	13,50
FLT3	4	A	7	10,67
FLT3	4	A	8	8,24
FLT3	4	A	9	8,76
FLT3	4	A	10	5,94
FLT4	2	H	9	48,87
FLT4	2	H	10	44,81
FLT4	2	H	11	40,98
FLT4	2	H	12	24,47
FLT4	3	A	1	16,13
FOS	5	B	4	27,55
FOS	5	B	5	24,93
FOS	5	B	6	36,07
FOS	5	B	7	20,37
FOS	5	B	8	9,12
GLI1	5	B	9	16,08
GLI1	5	B	10	20,25
GLI1	5	B	11	10,14
GLI1	5	B	12	6,49
GLI1	5	C	1	27,12
GLI2	5	C	2	23,66
GLI2	5	C	3	55,54
GLI2	5	C	4	28,05
GLI2	5	C	5	31,35
HDAC1	4	E	8	17,47
HDAC1	4	E	9	6,50
HDAC1	4	E	10	12,23
HDAC1	4	E	11	16,67
HDAC1	4	E	12	6,77
HDAC2	2	B	6	29,92
HDAC2	2	B	7	35,92
HDAC2	2	B	8	43,07
HDAC2	2	B	9	54,33
HDAC2	2	B	10	64,93
HDAC6	5	G	2	30,21
HDAC6	5	G	3	29,20
HDAC6	5	G	4	49,02
HDAC6	5	G	5	34,52
HDAC6	5	G	6	54,04
HIF1A	8	C	2	34,13
HIF1A	8	C	3	16,11
HRAS	5	C	6	30,54
HRAS	5	C	7	31,72
HRAS	5	C	8	16,12
HRAS	5	C	9	17,50
HRAS	5	C	10	25,38
IDH1	5	E	2	29,98

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GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
IDH1	5	E	3	42,91
IDH1	5	E	4	38,23
IDH1	5	E	5	27,67
IDH1	5	E	6	28,95
IDH2	3	A	2	9,22
IDH2	3	A	3	19,46
IDH2	3	A	4	21,64
IDH2	3	A	5	4,32
IDH2	3	A	6	23,11
IGF1R	1	D	5	73,28
IGF1R	1	D	6	80,45
IGF1R	1	D	7	45,88
IGF1R	1	D	8	86,27
IGF1R	1	D	9	38,92
IKBKB	2	B	11	70,61
IKBKB	2	B	12	29,58
IKBKB	2	C	1	23,66
IKBKB	2	C	2	13,84
IKBKB	2	C	3	23,47
IL17RA	6	C	10	10,67
IL17RA	6	C	11	16,62
IL17RA	6	C	12	10,23
IL17RA	6	D	1	100,00
IL17RA	6	D	2	56,29
IRF4	8	D	1	12,80
IRF4	8	D	2	21,31
IRF4	8	D	3	12,61
JAK2	4	F	1	25,69
JAK2	4	F	2	34,96
JAK2	4	F	3	47,36
JAK2	4	F	4	40,19
JAK2	4	F	5	29,51
JAK3	1	A	6	35,49
JAK3	1	A	7	6,41
JAK3	1	A	8	50,03
JAK3	1	A	9	24,55
JAK3	1	A	10	61,30
JUN	3	A	7	15,14
JUN	3	A	8	12,87
JUN	3	A	9	29,70
JUN	3	A	10	12,44
JUN	3	A	11	16,01
KDM1A	6	D	6	22,49
KDM1A	6	D	7	35,67
KDM1A	6	D	8	21,16
KDM1A	6	D	9	33,28
KDM1A	6	D	10	15,32
KDR	3	A	12	7,34

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
KDR	3	B	1	20,94
KDR	3	B	2	41,94
KDR	3	B	3	11,55
KDR	3	B	4	74,49
KIT	1	A	11	23,79
KIT	1	A	12	7,84
KIT	1	B	1	20,07
KIT	1	B	2	26,16
KIT	1	B	3	49,32
KRAS	4	F	6	20,59
KRAS	6	H	3	42,76
KRAS	6	H	4	29,58
KRAS	6	H	5	24,40
KRAS	6	H	6	19,53
LDHA	5	D	4	44,28
LDHA	5	D	5	37,21
LDHA	5	D	6	27,02
LDHA	5	D	7	24,31
LDHA	5	D	8	15,58
LEF1	8	E	6	25,80
LEF1	8	E	7	55,07
LTA4H	1	D	10	58,37
LTA4H	1	D	11	49,56
LTA4H	1	D	12	13,59
LTA4H	1	E	1	19,05
LTA4H	1	E	2	22,89
LTC4S	1	E	3	27,52
LTC4S	1	E	4	40,68
LTC4S	1	E	5	54,50
LTC4S	1	E	6	76,22
MAFF	8	A	8	29,84
MAFF	8	A	9	42,11
MAFF	8	A	10	6,16
MAFF	8	A	11	31,44
MAFF	8	A	12	22,88
MAML2	6	G	5	38,41
MAML2	6	G	6	24,55
MAML2	6	G	7	38,21
MAML2	6	G	8	28,87
MAML2	6	G	9	24,80
MAPK14	2	A	3	16,06
MAPK14	2	A	4	40,18
MAPK14	2	A	5	44,11
MAPK14	2	A	6	29,33
MAPK14	2	A	7	22,20
MAPK8	6	H	12	8,80
MAPK9	3	C	12	4,64
MAPK9	3	D	1	5,50

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
MAPK9	3	D	2	29,91
MAPK9	3	D	3	20,70
MAPK9	3	D	4	58,35
MCL1	6	E	4	57,63
MCL1	6	E	5	86,29
MCL1	6	E	6	35,07
MCL1	6	E	7	21,14
MCL1	6	E	8	24,01
MDM2	3	B	5	23,11
MDM2	3	B	6	68,91
MDM2	3	B	7	25,11
MDM2	3	B	8	62,90
MET	1	B	4	55,31
MET	1	B	5	87,99
MET	1	B	6	56,48
MET	1	B	7	52,09
MET	1	B	8	5,14
MLL	5	F	5	33,17
MLL	5	F	6	27,81
MLL	5	F	7	18,57
MLL	5	F	8	23,86
MLL	5	F	9	18,26
MLL2	3	G	11	20,83
MLL2	3	G	12	12,91
MLL2	3	H	1	23,08
MLL2	3	H	2	20,13
MLL2	3	H	3	7,59
MTOR	4	E	3	32,16
MTOR	4	E	4	48,89
MTOR	4	E	5	55,96
MTOR	4	E	6	32,12
MTOR	4	E	7	21,65
MYC	3	B	9	32,85
MYC	3	B	10	19,53
MYC	3	B	11	29,53
MYC	3	B	12	5,23
MYC	3	C	1	21,59
NANOG	8	C	8	50,74
NANOG	8	C	9	69,37
NANOG	8	C	10	5,04
NANOG	8	C	11	30,50
NANOG	8	C	12	25,88
NFKB1	8	C	4	2,28
NFKB1	8	C	5	9,90
NFKB1	8	C	6	21,06
NFKB1	8	C	7	36,22
NFKB2	3	C	2	44,86
NFKB2	3	C	3	24,08

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
NFKB2	3	C	4	46,49
NFKB2	3	C	5	16,56
NFKB2	3	C	6	93,19
NOTCH1	6	D	11	6,81
NOTCH1	6	D	12	8,22
NOTCH1	6	E	1	53,38
NOTCH1	6	E	2	46,41
NOTCH1	6	E	3	63,11
NOTCH3	1	B	9	44,09
NOTCH3	1	B	10	92,41
NOTCH3	1	B	11	20,91
NOTCH3	1	B	12	45,89
NOTCH3	1	C	1	15,74
NRAS	3	C	7	31,98
NRAS	3	C	8	54,33
NRAS	3	C	9	52,69
NRAS	3	C	10	15,74
NRAS	3	C	11	50,55
PARP1	2	C	4	45,35
PARP1	2	C	5	46,98
PARP1	2	C	6	47,09
PARP1	2	C	7	40,99
PARP1	2	C	8	49,01
PDGFRA	8	F	8	65,45
PDGFRA	8	F	9	76,41
PDGFRA	8	F	10	39,29
PDGFRA	8	F	11	2,22
PDGFRA	8	F	12	7,84
PDGFRB	8	F	3	12,70
PDGFRB	8	F	4	6,04
PDGFRB	8	F	5	38,82
PDGFRB	8	F	6	42,65
PDGFRB	8	F	7	25,04
PIK3CA	5	G	7	34,87
PIK3CA	5	G	8	32,02
PIK3CA	5	G	9	35,27
PIK3CA	5	G	10	17,16
PIK3CA	5	G	11	10,54
PLK1	4	F	7	17,41
PLK1	4	F	8	9,62
PLK1	4	F	9	13,97
PLK1	4	F	10	12,98
PLK1	4	F	11	11,45
POU5F1B	1	F	5	100,00
POU5F1B	1	F	6	22,64
POU5F1B	1	F	7	8,10
POU5F1B	1	F	8	27,64
POU5F1B	1	F	9	16,65

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
PPARGC1A	6	C	5	13,11
PPARGC1A	6	C	6	24,29
PPARGC1A	6	C	7	11,83
PPARGC1A	6	C	8	20,72
PPARGC1A	6	C	9	17,32
PTGER2	1	E	7	29,73
PTGER2	1	E	8	90,02
PTGER2	1	E	9	23,23
PTGER2	1	E	10	33,94
PTGER2	1	E	11	43,85
PTGES	4	D	10	14,00
PTGES	4	D	11	15,01
PTGES	4	D	12	5,93
PTGES	4	E	1	17,84
PTGES	4	E	2	41,83
PTK2	5	D	9	13,47
PTK2	5	D	10	23,80
PTK2	5	D	11	12,45
PTK2	5	D	12	8,67
PTK2	5	E	1	53,85
RAC1	8	A	3	10,57
RAC1	8	A	4	14,37
RAC1	8	A	5	31,24
RAC1	8	A	6	18,47
RAC1	8	A	7	32,06
RAC2	3	D	5	8,55
RAC2	3	D	6	59,44
RAC2	3	D	7	56,94
RAC2	3	D	8	28,14
RAC2	3	D	9	28,73
RAC3	4	F	12	7,09
RAC3	4	G	1	40,92
RAC3	4	G	2	53,56
RAC3	4	G	3	55,97
RAC3	4	G	4	44,47
RAF1	3	D	10	21,01
RAF1	3	D	11	28,29
RAF1	3	D	12	10,46
RAF1	3	E	1	25,57
RAF1	3	E	2	53,09
REL	3	E	3	32,84
REL	3	E	4	26,09
REL	3	E	5	8,58
REL	3	E	6	4,02
REL	3	E	7	28,88
RELA	6	E	9	24,37
RELA	6	E	10	12,13
RELA	6	E	11	11,39

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
RELA	6	E	12	6,29
RELA	6	F	1	47,38
RELB	5	H	1	33,98
RELB	5	H	2	28,04
RELB	5	H	3	25,62
RELB	5	H	4	22,54
RELB	5	H	5	17,77
RHO	1	C	7	34,34
RHO	1	C	8	72,44
RHO	1	C	9	45,95
RHO	1	C	10	84,71
RHO	1	C	11	46,57
ROS1	3	E	8	57,89
ROS1	3	E	9	44,14
ROS1	3	E	10	11,75
ROS1	3	E	11	23,80
ROS1	3	E	12	6,37
RPS6	1	E	12	28,42
RPS6	1	F	1	7,07
RPS6	1	F	2	10,09
RPS6	1	F	3	28,15
RPS6	1	F	4	3,49
RUNX1	2	D	7	39,78
RUNX1	2	D	8	51,66
RUNX1	2	D	9	61,01
RUNX1	2	D	10	62,79
RUNX1	2	D	11	77,93
RUNX2	4	B	9	15,54
SGK	8	B	3	8,37
SGK	8	B	4	12,01
SGK	8	B	5	21,78
SGK	8	B	6	27,73
SGK	8	B	7	45,38
SIRT1	6	B	7	34,20
SIRT1	6	B	8	19,72
SIRT1	6	B	9	8,25
SIRT1	6	B	10	19,21
SIRT1	6	B	11	17,01
SKP2	5	F	10	18,06
SKP2	5	F	11	9,88
SKP2	5	F	12	7,48
SKP2	5	G	1	34,99
SLC2A1	5	H	6	23,46
SLC2A1	5	H	7	22,85
SLC2A1	5	H	8	21,59
SLC2A1	5	H	9	19,10
SLC2A1	5	H	10	13,17
SMAD2	5	E	7	29,12

Table S4

GENE SYMBOL	PLATE Number	PLATE ROW	PLATE COLUMN	T
SMAD2	5	E	8	31,76
SMAD2	5	E	9	19,89
SMAD2	5	E	10	18,72
SMAD2	5	E	11	10,91
SMAD3	5	E	12	6,33
SMAD3	5	F	1	36,01
SMAD3	5	F	2	28,03
SMAD3	5	F	3	43,55
SMAD3	5	F	4	28,14
SMAD4	5	C	11	8,98
SMAD4	5	C	12	7,16
SMAD4	5	D	1	35,62
SMAD4	5	D	2	43,73
SMAD4	5	D	3	33,08
SMO	8	D	9	67,62
SMO	8	D	10	19,33
SMO	8	D	11	40,23
SMO	8	D	12	21,05
SMO	8	E	1	14,92
SNAI2	3	F	1	18,78
SNAI2	3	F	2	9,87
SNAI2	3	F	3	21,79
SNAI2	3	F	4	55,40
SNAI2	3	F	5	11,99
SOX2	8	E	8	91,06
SOX2	8	E	9	46,49
SRCIN1	6	F	7	33,21
SRCIN1	6	F	8	24,31
SRCIN1	6	F	9	24,37
SRCIN1	6	F	10	11,86
SRCIN1	6	F	11	7,88
STAT1	6	A	9	12,26
STAT1	6	A	10	11,10
STAT1	6	A	11	11,04
STAT1	6	A	12	9,47
STAT1	6	B	1	44,02
STAT3	8	B	8	24,04
STAT3	8	B	9	24,82
STAT3	8	B	10	4,71
STAT5A	3	F	6	83,99
STAT5A	3	F	7	42,00
STAT5A	3	F	8	48,02
STAT5A	3	F	9	43,35
STAT5A	3	F	10	16,50
STAT5B	6	B	12	12,73
STAT5B	6	C	1	68,94
STAT5B	6	C	2	34,59
STAT5B	6	C	3	43,07

Table S4

GENE_SYMBOL	PLATE_Number	PLATE_ROW	PLATE_COLUMN	T
STAT5B	6	C	4	34,93
TCF4	3	F	11	32,75
TCF4	3	F	12	11,94
TCF4	3	G	1	17,81
TCF4	3	G	2	27,43
TCF4	3	G	3	12,08
TERT	3	G	4	36,30
TERT	3	G	5	15,82
TNS4	6	G	10	15,28
TNS4	6	G	11	7,97
TNS4	6	G	12	17,97
TNS4	6	H	1	39,28
TNS4	6	H	2	44,79
TRAF6	4	C	12	7,43
TRAF6	4	D	1	53,45
TRAF6	4	D	2	48,18
TRAF6	4	D	3	55,39
TRAF6	4	D	4	12,88
TWIST1	1	C	2	18,87
TWIST1	1	C	3	28,78
TWIST1	1	C	4	33,63
TWIST1	1	C	5	49,21
TWIST1	1	C	6	53,19
UBE2D2	3	G	6	44,62
UBE2D2	3	G	7	38,47
UBE2D2	3	G	8	8,92
UBE2D2	3	G	9	36,31
UBE2D2	3	G	10	13,75
XIAP	1	G	8	72,53
XIAP	1	G	9	23,32
XIAP	1	G	10	5,70
XIAP	1	G	11	43,97
XIAP	1	G	12	25,85
ZEB1	6	F	12	13,82
ZEB1	6	G	1	40,53
ZEB1	6	G	2	41,67
ZEB1	6	G	3	48,44
ZEB1	6	G	4	32,63

Table S4

CTRL_ID	PuroSelection			T
CTRL_PURO_20	+			100,00
CTRL_PURO_10	+			100,00
CTRL_PURO_5	+			68,55
CTRL_PURO_1	+			27,73
CTRL_GFP_20	-			100,00
CTRL_GFP_20	-			100,00
CTRL_GFP_10	-			100,00
CTRL_GFP_10	-			100,00
CTRL_67C_20	+			37,52
CTRL_67C_10	+			29,00
NT	-			99,93
NT	-			100,00
NT	-			84,70
NT	-			100,00
NT	+			4,17
NT	+			4,49

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
ABL1	G5	88,56	16,86
ABL1	G6	55,01	2,74
ABL1	G7	30,42	1,35
ABL1	G8	51,89	6,19
ABL2	G10	99,00	2,38
ABL2	G11	12,04	2,57
ABL2	H1	0,85	0,18
ABL2	H2	1,15	0,16
AKT1	H3	1,47	0,21
AKT1	H4	1,69	0,11
AKT1	H5	1,22	0,05
AKT1	H6	2,10	0,03
AKT1	H7	6,17	0,10
AKT2	C9	0,04	0,01
AKT2	C10	0,22	0,06
AKT2	C11	0,20	0,02
AKT2	C12	0,22	0,05
AKT2	D1	0,87	0,91
ARNT	D2	1,10	2,61
ARNT	D3	2,95	2,01
ARNT	D4	0,90	0,52
ARNT	D5	0,42	0,20
ARNT	D6	0,43	0,18
ATF1	H8	8,47	0,10
ATF1	H9	7,59	0,00
ATF1	H10	9,35	0,00
ATF3	G10	0,24	0,04
ATG5	D5	65,47	2,90
ATG5	D6	54,48	8,80
ATG5	D7	22,47	0,98
AURKB	B1	51,90	14,06
AURKB	B2	63,40	13,91
AURKB	B3	217,83	30,42
BCAR1	D3	182,64	53,06
BCAR1	D4	17,36	0,69
BCAR1	D5	102,68	7,86
BCL2	C12	0,60	0,14
BCL2	D1	4,77	3,55
BCL2	D2	4,33	5,54
BCL2	D3	1,73	0,14
BCL2	D4	3,70	0,71
BCL2A1	G12	0,92	0,72
BCL2A1	H1	0,34	0,34
BCL3	D5	4,25	0,42
BCL3	D6	2,08	0,35
BCL3	D7	0,46	0,07
BECN1	H4	1,07	0,31
BECN1	H5	0,42	0,16

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
BECN1	H6	2,38	2,32
BECN1	H7	1,69	1,00
BIRC2	G3	0,25	0,02
BIRC2	G4	2,60	0,77
BIRC2	G5	0,86	0,15
BIRC2	G6	2,73	1,57
BIRC2	G7	3,34	0,45
BIRC3	F10	2,27	0,51
BIRC3	F11	2,86	4,53
BIRC3	F12	1,94	0,87
BIRC3	G1	2,47	0,28
BIRC3	G2	3,80	5,21
BRAF	B4	65,46	9,15
BRAF	B5	57,88	5,88
BRAF	B6	77,45	1,56
BRAF	B7	54,71	4,13
BRAF	B8	108,76	21,30
BTRC	A2	262,26	128,93
BTRC	A3	170,54	10,90
BTRC	A4	123,36	33,63
BTRC	A5	103,02	3,14
C/EBP BETA	B1	1,65	0,43
C/EBP BETA	B2	1,17	0,32
CA9	H1	6,27	1,35
CA9	H2	3,43	0,69
CA9	H4	3,26	1,01
CA9	H5	3,10	2,65
CBFB	D12	0,46	0,11
CBFB	E1	0,64	0,71
CBFB	E2	0,68	0,19
CBFB	E3	0,53	0,12
CBFB	E4	1,62	1,44
CCND1	H7	46,51	2,19
CCND1	H8	28,58	1,45
CCND1	H9	30,66	0,88
CCND1	H10	45,20	1,32
CCND1	H11	35,60	3,44
CDC42	A2	0,79	0,12
CDH2	E10	1,10	0,84
CDH2	E11	0,41	0,14
CDH2	E12	0,27	0,16
CDH2	F1	3,08	1,74
CDH2	F2	2,15	3,85
CDK1	E5	1,64	1,15
CDK1	E6	0,61	0,09
CDK1	E7	1,01	0,60
CDK1	E8	3,57	9,24
CDK1	E9	0,50	0,91

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
CDK2	F3	0,47	0,16
CDK2	F4	0,39	0,07
CDK2	F6	0,83	0,04
CDK2	F7	1,44	2,41
CDK4	A1	0,35	0,07
CDK4	A2	2,73	2,99
CDK4	A3	0,86	0,03
CDK4	A4	0,62	0,04
CDK4	A5	1,54	0,27
CDK6	H7	1,28	0,11
CDK6	H8	1,46	0,26
CDK6	H9	4,80	0,41
CDK7	F8	0,25	0,06
CDK7	F9	0,16	0,04
CDK7	F10	0,17	0,04
CDK7	F11	1,07	2,92
CDK7	F12	0,10	0,05
CFLAR	A1	115,15	25,26
CFLAR	H9	1,32	0,83
CFLAR	H12	0,90	0,55
CHUK	H10	2,72	0,19
CHUK	H11	1,07	0,06
CHUK	H12	0,79	0,08
CHUK	A2	0,28	0,24
CIP1	B11	1,33	0,45
CIP1	B12	0,20	0,05
CIP1	C1	1,52	0,21
CREB1	B10	86,39	3,50
CREB1	B11	31,81	4,92
CREB1	C1	61,94	37,33
CREB1	C2	90,19	12,60
CTNNB1	G1	0,36	0,06
CTNNB1	G2	0,33	0,15
CTNNB1	G3	1,12	2,35
CTNNB1	G4	2,75	5,43
CTNNB1	G5	0,49	0,11
CYSLTR1	A1	160,86	16,71
CYSLTR1	A2	133,43	6,11
CYSLTR1	A3	227,04	62,08
DNMT1	A8	1,36	1,37
DNMT1	A9	1,19	0,83
DNMT1	A10	1,28	0,76
DNMT1	A11	0,95	1,28
DNMT1	A12	2,55	3,67
DNMT3A	F2	119,38	16,88
DNMT3A	F3	117,61	19,32
DNMT3A	F4	213,43	11,71
DNMT3A	F5	126,39	21,74

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
DNMT3A	F6	251,75	14,80
DNMT3B	A4	200,92	54,41
DNMT3B	A5	169,15	10,56
DNMT3B	A6	176,79	1,65
DNMT3B	A7	24,09	0,82
DNMT3B	A8	19,61	1,17
E2F1	A1	145,14	50,51
E2F1	A2	110,98	18,19
E2F1	A3	35,03	2,12
E2F1	A4	64,38	6,30
E2F1	A5	28,08	2,55
EGFR	A6	35,19	8,48
EGFR	A7	29,33	1,05
EGFR	A8	12,34	5,27
EGFR	A9	23,59	1,24
EGFR	A10	12,94	0,71
EIF4B	B2	0,25	0,05
EIF4B	B3	0,72	0,18
EIF4B	B4	4,01	0,57
EIF4B	B5	0,61	0,17
EIF4E	G6	1,50	0,76
EIF4E	G7	2,51	5,34
EIF4E	G8	3,78	16,50
EIF4E	G9	0,66	0,60
EIF4E	G10	1,06	0,41
ERBB2	C3	86,59	14,10
ERBB2	C4	96,70	11,95
ERBB2	C5	74,84	12,94
ERBB2	C6	17,30	1,13
ERBB2	C7	36,34	0,79
ERBB3	G11	0,15	0,05
ERBB3	G12	1,31	1,12
ERBB3	H1	0,65	0,13
ERBB3	H3	1,49	6,92
ERBB4	B1	180,01	53,19
ERBB4	B2	85,15	25,02
ERBB4	B3	126,25	35,36
ETS1	E2	1,00	0,64
ETS1	E3	2,06	0,73
EZH2	C8	44,54	5,31
EZH2	C9	30,32	2,90
EZH2	C11	34,04	10,79
FBXO5	B2	206,75	22,94
FBXO5	B3	76,55	10,60
FBXO5	B4	93,93	16,95
FBXO5	B5	61,02	1,53
FBXO5	B6	121,21	1,65
FLI1	E4	0,43	0,17

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
FLI1	E5	2,91	1,29
FLT1	H4	0,81	0,17
FLT1	H5	0,36	0,10
FLT1	H6	0,21	0,03
FLT1	H7	0,71	0,49
FLT1	H8	0,91	0,88
FLT3	A6	46,75	8,02
FLT3	A7	75,10	12,88
FLT4	H9	0,05	0,01
FLT4	H10	0,95	0,42
FLT4	H11	0,12	0,02
FLT4	H12	0,31	0,07
FLT4	A1	2,31	0,59
FOS	B4	26,40	1,18
FOS	B5	52,78	5,93
FOS	B6	107,52	35,19
FOS	B7	44,66	21,57
GLI1	B9	23,19	0,99
GLI1	B10	12,93	0,87
GLI1	C1	66,59	29,19
GLI2	C2	79,16	26,83
GLI2	C3	31,23	7,68
GLI2	C4	54,29	4,58
GLI2	C5	72,95	9,57
HDAC1	E8	64,26	17,19
HDAC1	E10	129,82	3,16
HDAC1	E11	33,41	2,68
HDAC2	B6	4,38	0,49
HDAC2	B7	0,98	0,75
HDAC2	B8	1,68	1,53
HDAC2	B9	0,22	0,02
HDAC2	B10	0,65	0,34
HDAC6	G2	80,52	13,80
HDAC6	G3	68,76	22,44
HDAC6	G4	54,94	12,63
HDAC6	G5	59,10	32,37
HDAC6	G6	11,19	0,24
HIF1A	C2	2,61	6,75
HIF1A	C3	0,47	0,21
HIF2/EPAS1	G1	2,59	2,19
HIF2/EPAS1	G2	1,37	1,08
HIF2/EPAS1	G3	2,53	0,46
HIF2/EPAS1	G6	1,09	0,63
HRAS	C6	60,87	21,42
HRAS	C7	16,50	0,41
HRAS	C8	26,75	2,94
HRAS	C9	36,08	1,94
HRAS	C10	32,89	0,98

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
IDH1	E2	93,21	16,22
IDH1	E3	77,58	24,23
IDH1	E4	158,98	26,04
IDH1	E5	91,43	15,46
IDH1	E6	60,78	7,19
IDH2	A3	1,41	0,16
IDH2	A4	0,23	0,10
IDH2	A6	0,60	0,13
IGF1R	D5	5,10	8,19
IGF1R	D6	3,28	3,23
IGF1R	D7	2,61	0,31
IGF1R	D8	1,17	0,40
IGF1R	D9	4,64	1,64
IKBKB	B11	0,37	0,44
IKBKB	B12	0,22	0,07
IKBKB	C1	0,51	0,10
IKBKB	C2	0,92	0,11
IKBKB	C3	0,72	0,18
IL17RA	C10	41,58	1,99
IL17RA	C11	41,87	1,88
IL17RA	C12	108,15	17,43
IL17RA	D1	164,70	12,37
IL17RA	D2	235,66	69,66
IRF4	D1	0,53	0,48
IRF4	D2	2,70	4,77
IRF4	D3	0,93	0,62
JAK2	F1	184,82	91,95
JAK2	F2	134,41	94,27
JAK2	F3	13,92	0,89
JAK2	F4	175,64	21,46
JAK2	F5	103,21	9,38
JAK3	A6	2,62	1,11
JAK3	A8	0,61	0,05
JAK3	A9	1,89	0,26
JAK3	A10	0,75	0,12
JUN	A7	2,53	6,40
JUN	A8	1,33	0,60
JUN	A9	1,19	0,24
JUN	A10	3,46	3,45
JUN	A11	0,50	0,33
KDM1A	D6	414,07	23,59
KDM1A	D7	54,39	1,65
KDM1A	D8	65,77	1,57
KDM1A	D9	18,90	0,53
KDM1A	D10	21,61	1,19
KDR	B1	3,15	0,77
KDR	B2	3,06	24,05
KDR	B3	0,30	0,59

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
KDR	B4	0,40	0,14
KIT	A11	0,71	0,03
KIT	B1	2,04	0,96
KIT	B2	4,75	0,43
KIT	B3	2,16	0,77
KRAS	F6	119,54	10,39
KRAS	H3	170,52	7,70
KRAS	H4	163,50	5,63
KRAS	H5	193,65	36,16
KRAS	H6	82,93	5,76
LDHA	D4	59,05	23,83
LDHA	D5	81,90	22,76
LDHA	D6	8,78	1,18
LDHA	D7	49,84	17,52
LDHA	D8	43,76	8,96
LEF1	E6	0,49	0,16
LEF1	E7	2,62	4,12
LTA4H	D10	3,85	0,54
LTA4H	D11	3,38	0,57
LTA4H	D12	1,30	0,33
LTA4H	E1	3,20	1,19
LTA4H	E2	3,44	3,76
LTC4S	E3	10,55	25,50
LTC4S	E4	4,43	0,77
LTC4S	E5	2,41	0,99
LTC4S	E6	2,08	1,31
MAFF	A8	0,62	0,08
MAFF	A9	1,45	0,75
MAFF	A11	1,70	1,35
MAFF	A12	0,25	0,08
MAML2	G5	135,32	11,24
MAML2	G6	188,75	15,73
MAML2	G7	23,17	1,36
MAML2	G8	24,10	0,68
MAML2	G9	50,60	1,44
MAPK14	A3	6,04	31,24
MAPK14	A4	0,36	0,10
MAPK14	A5	1,41	1,30
MAPK14	A6	0,62	0,14
MAPK14	A7	0,52	0,14
MAPK9	D2	2,30	4,34
MAPK9	D3	2,22	1,13
MAPK9	D4	2,66	2,18
MCL1	E4	143,80	6,56
MCL1	E5	31,98	0,55
MCL1	E6	56,84	1,28
MCL1	E7	21,99	0,68
MCL1	E8	15,44	0,85

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
MDM2	B5	1,46	2,00
MDM2	B6	0,21	0,10
MDM2	B7	1,45	0,81
MDM2	B8	4,09	26,18
MET	B4	0,76	0,05
MET	B5	2,29	2,92
MET	B6	2,15	0,15
MET	B7	7,48	2,21
MLL	F5	50,22	4,12
MLL	F6	49,28	8,40
MLL	F7	6,18	0,43
MLL	F8	22,12	1,76
MLL	F9	15,78	0,43
MLL2	G11	0,52	0,65
MLL2	G12	1,81	0,48
MLL2	H1	0,85	0,30
MLL2	H2	2,47	0,63
MTOR	E3	49,45	3,90
MTOR	E4	121,45	10,33
MTOR	E5	5,68	0,30
MTOR	E6	42,16	3,65
MTOR	E7	49,73	1,09
MYC	B9	0,91	1,21
MYC	B10	4,76	9,81
MYC	B11	0,76	0,13
MYC	C1	2,06	5,33
NANOG	C8	0,41	0,14
NANOG	C9	1,15	0,44
NANOG	C11	2,56	3,81
NANOG	C12	0,71	0,18
NFKB1	C6	0,58	0,12
NFKB1	C7	0,47	0,10
NFKB2	C2	2,55	8,65
NFKB2	C3	0,64	0,48
NFKB2	C4	2,76	19,82
NFKB2	C5	3,78	8,62
NFKB2	C6	4,88	21,80
NOTCH1	E1	177,90	8,28
NOTCH1	E2	165,57	2,58
NOTCH1	E3	118,65	24,65
NOTCH3	B9	0,58	0,49
NOTCH3	B10	1,71	0,54
NOTCH3	B11	1,60	0,14
NOTCH3	B12	3,01	1,21
NOTCH3	C1	1,00	0,19
NRAS	C7	0,32	0,53
NRAS	C8	4,96	16,60
NRAS	C9	3,66	5,91

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
NRAS	C10	5,09	42,66
NRAS	C11	0,49	0,36
PARP1	C4	2,17	3,05
PARP1	C5	1,34	1,31
PARP1	C6	1,20	0,14
PARP1	C7	6,22	2,89
PARP1	C8	0,48	0,21
PDGFR a	F8	4,97	7,43
PDGFR a	F9	0,29	0,21
PDGFR a	F10	0,60	0,39
PDGFR b	F3	1,14	0,71
PDGFR b	F5	5,75	6,65
PDGFR b	F6	1,24	0,22
PDGFR b	F7	0,34	0,24
PIK3CA	G7	58,11	4,76
PIK3CA	G8	15,66	2,91
PIK3CA	G9	29,24	0,61
PIK3CA	G10	2,25	0,25
PIK3CA	G11	2,63	0,55
PLK1	F7	33,02	3,75
PLK1	F9	60,98	7,93
PLK1	F10	31,20	2,00
PLK1	F11	38,05	1,95
POU5F1B	F5	7,71	4,97
POU5F1B	F6	0,53	0,29
POU5F1B	F8	0,91	0,30
POU5F1B	F9	1,10	0,47
PPARGC1A	C5	40,80	1,22
PPARGC1A	C6	257,33	6,66
PPARGC1A	C7	39,80	1,18
PPARGC1A	C8	41,64	1,22
PPARGC1A	C9	40,86	0,81
PTGER2	E7	19,25	42,58
PTGER2	E8	2,69	1,58
PTGER2	E9	1,59	0,88
PTGER2	E10	1,52	0,15
PTGER2	E11	0,49	0,07
PTGES	D10	45,98	2,46
PTGES	D11	36,50	2,63
PTGES	E1	9,22	4,40
PTGES	E2	171,02	76,87
PTK2	D9	9,06	0,64
PTK2	D10	3,05	0,41
PTK2	D11	3,23	0,90
PTK2	E1	79,41	37,55
RAC1	A3	1,83	2,37
RAC1	A4	1,26	0,10
RAC1	A5	0,50	0,06

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
RAC1	A6	0,29	0,10
RAC1	A7	0,70	0,24
RAC2	D6	3,99	23,00
RAC2	D7	4,54	15,08
RAC2	D8	2,39	12,97
RAC2	D9	1,48	0,27
RAC3	G1	56,41	15,66
RAC3	G2	108,81	11,20
RAC3	G3	71,63	13,28
RAC3	G4	77,88	7,30
RAF1	D10	2,81	5,55
RAF1	D11	0,41	0,31
RAF1	D12	0,75	0,40
RAF1	E1	0,44	0,10
RAF1	E2	0,45	0,20
REL	E3	0,25	0,13
REL	E4	0,59	0,19
REL	E7	1,91	3,65
RELA	E9	14,84	0,69
RELA	E10	37,58	1,43
RELA	E11	25,33	2,01
RELA	F1	247,60	37,13
RELB	H1	37,90	2,39
RELB	H2	48,75	12,25
RELB	H3	43,62	12,22
RELB	H4	23,34	0,84
RELB	H5	20,14	1,91
RHO	C7	5,78	1,78
RHO	C8	0,28	0,02
RHO	C9	4,83	3,93
RHO	C10	4,93	2,86
RHO	C11	0,23	0,05
ROS1	E8	3,33	21,91
ROS1	E9	0,41	0,26
ROS1	E10	0,88	0,57
ROS1	E11	0,47	0,41
RPS6	E12	0,76	0,06
RPS6	F2	0,57	0,12
RPS6	F3	2,36	0,20
RUNX1	D7	1,49	1,07
RUNX1	D8	0,48	0,15
RUNX1	D9	0,27	0,10
RUNX1	D10	0,56	0,37
RUNX1	D11	0,33	0,06
RUNX2	B9	134,04	5,30
SGK	B4	0,55	0,31
SGK	B5	9,06	0,19
SGK	B6	2,28	9,86

Table S5

GENE SYMBOL	shRNA ID	GR D3	GR D7
SGK	B7	0,80	0,14
SIRT1	B7	38,74	6,15
SIRT1	B8	22,96	1,04
SIRT1	B10	20,24	0,70
SIRT1	B11	31,08	1,16
SKP2	F10	12,96	4,11
SKP2	G1	98,25	76,83
SLC2A1	H6	15,04	2,07
SLC2A1	H7	40,85	5,19
SLC2A1	H8	34,81	16,75
SLC2A1	H9	12,40	0,68
SLC2A1	H10	15,53	0,54
SMAD2	E7	54,30	2,04
SMAD2	E8	12,04	2,72
SMAD2	E9	18,22	0,76
SMAD2	E10	10,61	0,42
SMAD2	E11	10,91	2,55
SMAD3	F1	45,74	12,47
SMAD3	F2	68,41	22,75
SMAD3	F3	32,80	5,16
SMAD3	F4	38,46	6,36
SMAD4	D1	106,20	46,82
SMAD4	D2	47,59	7,91
SMAD4	D3	60,95	3,65
SMO	D9	1,94	1,52
SMO	D10	1,60	0,40
SMO	D11	1,23	0,62
SMO	D12	0,54	0,30
SMO	E1	0,75	0,16
SNAI2	F1	0,10	0,11
SNAI2	F3	0,90	0,99
SNAI2	F4	1,58	13,37
SNAI2	F5	1,04	1,15
SNFT	G7	0,81	0,31
SNFT	G8	1,40	0,45
SNFT	G9	1,13	2,70
SOX2	E8	0,20	0,05
SOX2	E9	0,31	0,08
SRCIN1	F7	51,97	0,80
SRCIN1	F8	101,71	4,24
SRCIN1	F9	19,20	0,69
SRCIN1	F10	35,85	1,09
STAT1	A9	28,00	1,24
STAT1	A10	29,55	1,42
STAT1	A11	110,95	1,86
STAT1	B1	40,58	1,87
STAT3	B8	1,15	0,36
STAT3	B9	0,11	0,03

Table S5

GENE_SYMBOL	shRNA_ID	GR_D3	GR_D7
STAT5A	F6	4,88	12,77
STAT5A	F7	0,88	2,41
STAT5A	F8	3,00	25,95
STAT5A	F9	2,46	7,59
STAT5A	F10	1,01	0,47
STAT5B	B12	33,90	5,13
STAT5B	C1	105,50	5,64
STAT5B	C2	44,67	1,70
STAT5B	C3	169,50	28,12
STAT5B	C4	183,97	7,80
TCF4	F11	2,77	6,11
TCF4	F12	1,30	0,56
TCF4	G1	1,85	1,43
TCF4	G2	3,14	3,22
TCF4	G3	0,90	1,59
TERT	G4	1,30	4,18
TERT	G5	0,30	0,23
TNS4	G10	38,37	0,83
TNS4	G12	38,55	2,32
TNS4	H1	72,17	5,38
TNS4	H2	151,09	8,87
TRAF6	D1	142,46	29,34
TRAF6	D2	161,87	34,61
TRAF6	D3	122,97	15,38
TRAF6	D4	27,10	4,99
TWIST1	C2	6,01	8,79
TWIST1	C3	2,33	1,62
TWIST1	C4	0,90	0,34
TWIST1	C5	0,96	0,34
TWIST1	C6	4,91	4,67
UBE2D2	G6	0,08	0,12
UBE2D2	G7	7,40	16,32
UBE2D2	G9	1,84	3,33
UBE2D2	G10	3,63	1,71
XIAP	G8	0,69	0,44
XIAP	G9	3,47	1,52
XIAP	G11	0,23	0,02
XIAP	G12	0,63	0,28
ZEB1	F12	47,94	4,63
ZEB1	G1	58,88	3,04
ZEB1	G2	111,56	30,22
ZEB1	G3	68,54	7,39
ZEB1	G4	175,22	4,88

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
ABL1	G5	-0,231	-0,681
ABL1	G6	-0,577	-0,810
ABL1	G7	-0,830	-0,823
ABL1	G8	-0,609	-0,779
ABL2	G10	-0,423	-0,825
ABL2	G11	-1,056	-0,824
ABL2	H1	-1,134	-0,834
ABL2	H2	-1,131	-0,834
AKT1	H3	-1,128	-0,834
AKT1	H4	-1,126	-0,835
AKT1	H5	-1,131	-0,835
AKT1	H6	-1,122	-0,835
AKT1	H7	-1,098	-0,835
AKT2	C9	-1,104	-0,833
AKT2	C10	-0,871	-0,818
AKT2	C11	-0,897	-0,830
AKT2	C12	-0,914	-0,826
AKT2	D1	-0,464	-0,743
ARNT	D2	-0,018	-0,293
ARNT	D3	1,857	-0,418
ARNT	D4	-0,016	-0,670
ARNT	D5	-0,622	-0,773
ARNT	D6	-0,702	-0,798
ATF1	H8	-1,082	-0,835
ATF1	H9	-1,088	-0,836
ATF1	H10	-1,075	-0,836
ATF3	G10	-0,949	-0,830
ATG5	D5	-0,469	-0,809
ATG5	D6	-0,582	-0,755
ATG5	D7	-0,912	-0,827
AURKB	B1	-0,766	-0,775
AURKB	B2	-0,490	-0,708
AURKB	B3	1,099	-0,557
BCAR1	D3	0,574	0,513
BCAR1	D4	-0,980	-0,818
BCAR1	D5	-0,178	-0,636
BCL2	C12	-0,824	-0,809
BCL2	D1	1,419	-0,181
BCL2	D2	1,181	0,186
BCL2	D3	-0,215	-0,810
BCL2	D4	1,297	-0,622
BCL2A1	G12	-0,629	-0,811
BCL2A1	H1	-0,955	-0,824
BCL3	D5	2,329	-0,776
BCL3	D6	0,297	-0,804
BCL3	D7	-0,771	-0,826
BECN1	H4	-0,411	-0,822

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
BECN1	H5	-0,853	-0,828
BECN1	H6	0,480	-0,733
BECN1	H7	0,014	-0,791
BIRC2	G3	-0,975	-0,828
BIRC2	G4	0,251	-0,693
BIRC2	G5	-0,577	-0,790
BIRC2	G6	0,657	-0,361
BIRC2	G7	0,651	-0,752
BIRC3	F10	0,358	-0,682
BIRC3	F11	0,744	0,531
BIRC3	F12	-0,101	-0,675
BIRC3	G1	0,182	-0,784
BIRC3	G2	0,899	0,126
BRAF	B4	-0,469	-0,752
BRAF	B5	-0,547	-0,782
BRAF	B6	-0,346	-0,821
BRAF	B7	-0,745	-0,818
BRAF	B8	-0,352	-0,744
BTRC	A2	1,557	0,345
BTRC	A3	0,613	-0,736
BTRC	A4	-0,246	-0,691
BTRC	A5	-0,083	-0,807
C/EBP BETA	B1	0,003	-0,797
C/EBP BETA	B2	-0,331	-0,807
CA9	H1	2,225	-0,586
CA9	H2	0,702	-0,708
CA9	H4	0,607	-0,649
CA9	H5	0,523	-0,347
CBFB	D12	-0,672	-0,813
CBFB	E1	-0,487	-0,689
CBFB	E2	-0,452	-0,795
CBFB	E3	-0,724	-0,824
CBFB	E4	0,503	-0,535
CCND1	H7	-0,873	-0,801
CCND1	H8	-0,977	-0,812
CCND1	H9	-0,965	-0,822
CCND1	H10	-0,880	-0,815
CCND1	H11	-0,936	-0,781
CDC42	A2	-0,592	-0,825
CDH2	E10	-0,027	-0,662
CDH2	E11	-0,635	-0,790
CDH2	E12	-0,934	-0,820
CDH2	F1	1,267	-0,659
CDH2	F2	1,042	-0,036
CDK1	E5	0,911	-0,473
CDK1	E6	-0,524	-0,817
CDK1	E7	-0,118	-0,710

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
CDK1	E8	2,491	1,085
CDK1	E9	-0,522	-0,550
CDK2	F3	-0,773	-0,820
CDK2	F4	-0,751	-0,821
CDK2	F6	-0,294	-0,827
CDK2	F7	0,324	-0,334
CDK4	A1	-0,957	-0,822
CDK4	A2	0,325	-0,283
CDK4	A3	-0,679	-0,830
CDK4	A4	-0,808	-0,829
CDK4	A5	-0,315	-0,787
CDK6	H7	-0,454	-0,815
CDK6	H8	-0,177	-0,756
CDK6	H9	-0,365	-0,760
CDK7	F8	-0,831	-0,818
CDK7	F9	-0,943	-0,824
CDK7	F10	-0,926	-0,823
CDK7	F11	0,195	0,081
CDK7	F12	-1,017	-0,819
CFLAR	A1	0,042	-0,604
CFLAR	H9	-0,240	-0,799
CFLAR	H12	-0,532	-0,811
CHUK	H12	1,436	-0,800
CHUK	H10	0,315	-0,824
CHUK	H11	-0,568	-0,820
CHUK	A2	-0,923	-0,811
CIP1	B11	-0,221	-0,795
CIP1	B12	-1,007	-0,831
CIP1	C1	-0,090	-0,816
CREB1	B10	-0,515	-0,820
CREB1	B11	-0,912	-0,814
CREB1	C1	-0,506	-0,494
CREB1	C2	-0,215	-0,720
CTNNB1	G1	-0,775	-0,822
CTNNB1	G2	-0,881	-0,820
CTNNB1	G3	0,001	-0,348
CTNNB1	G4	1,657	0,293
CTNNB1	G5	-0,641	-0,813
CYSLTR1	A1	-0,207	-0,569
CYSLTR1	A2	-0,128	-0,709
CYSLTR1	A3	0,584	0,447
DNMT1	A8	-0,080	-0,697
DNMT1	A9	0,067	-0,662
DNMT1	A10	0,455	-0,596
DNMT1	A11	0,045	-0,433
DNMT1	A12	1,455	-0,073
DNMT3A	F2	-0,021	-0,407

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
DNMT3A	F3	-0,038	-0,345
DNMT3A	F4	0,481	-0,594
DNMT3A	F5	0,045	-0,283
DNMT3A	F6	0,322	-0,600
DNMT3B	A4	0,386	0,289
DNMT3B	A5	-0,159	-0,667
DNMT3B	A6	-0,114	-0,809
DNMT3B	A7	-1,003	-0,823
DNMT3B	A8	-1,029	-0,817
E2F1	A1	3,161	0,285
E2F1	A2	2,148	-0,432
E2F1	A3	-0,104	-0,789
E2F1	A4	0,766	-0,696
E2F1	A5	-0,311	-0,779
EGFR	A6	-0,100	-0,647
EGFR	A7	-0,273	-0,812
EGFR	A8	-0,777	-0,719
EGFR	A9	-0,444	-0,808
EGFR	A10	-0,760	-0,820
EIF4B	B2	-0,888	-0,825
EIF4B	B3	-0,411	-0,799
EIF4B	B4	3,881	-0,657
EIF4B	B5	-0,375	-0,781
EIF4E	G6	0,029	-0,758
EIF4E	G7	1,411	0,275
EIF4E	G8	2,708	2,594
EIF4E	G9	-0,312	-0,648
EIF4E	G10	0,189	-0,705
ERBB2	C3	-0,252	-0,706
ERBB2	C4	-0,148	-0,726
ERBB2	C5	-0,147	-0,654
ERBB2	C6	-0,965	-0,825
ERBB2	C7	-0,769	-0,828
ERBB3	G11	-0,960	-0,820
ERBB3	G12	0,499	-0,483
ERBB3	H1	-0,637	-0,822
ERBB3	H3	0,025	-0,134
ERBB4	B1	4,195	0,345
ERBB4	B2	1,382	-0,280
ERBB4	B3	2,601	-0,051
ETS1	E2	-0,449	-0,778
ETS1	E3	0,288	-0,770
EZH2	C8	-0,819	-0,813
EZH2	C9	-0,923	-0,823
EZH2	C11	-0,896	-0,789
FBXO5	B2	0,430	-0,361
FBXO5	B3	-0,424	-0,566

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
FBXO5	B4	-0,260	-0,405
FBXO5	B5	-0,788	-0,811
FBXO5	B6	-0,221	-0,801
FLI1	E4	-0,848	-0,820
FLI1	E5	1,237	-0,650
FLT1	H4	-0,316	-0,800
FLT1	H5	-0,774	-0,815
FLT1	H6	-0,925	-0,830
FLT1	H7	-0,422	-0,733
FLT1	H8	-0,220	-0,653
FLT3	A6	-0,803	-0,801
FLT3	A7	-0,597	-0,780
FLT4	H9	-1,082	-0,833
FLT4	H10	-0,176	-0,748
FLT4	H11	-1,017	-0,831
FLT4	H12	-0,830	-0,822
FLT4	A1	0,431	-0,809
FOS	B4	-0,360	-0,809
FOS	B5	0,422	-0,704
FOS	B6	2,045	-0,055
FOS	B7	0,181	-0,357
GLI1	B9	-0,455	-0,814
GLI1	B10	-0,760	-0,816
GLI1	C1	0,831	-0,188
GLI2	C2	1,204	-0,240
GLI2	C3	0,303	-0,569
GLI2	C4	0,467	-0,734
GLI2	C5	1,020	-0,623
HDAC1	E8	-0,676	-0,762
HDAC1	E10	-0,199	-0,822
HDAC1	E11	-0,900	-0,824
HDAC2	B6	3,318	-0,734
HDAC2	B7	-0,147	-0,680
HDAC2	B8	0,569	-0,518
HDAC2	B9	-0,869	-0,828
HDAC2	B10	-0,329	-0,729
HDAC6	G2	1,244	-0,529
HDAC6	G3	0,896	-0,338
HDAC6	G4	1,402	-0,397
HDAC6	G5	0,609	-0,117
HDAC6	G6	-0,625	-0,827
HIF1A	C2	0,985	0,138
HIF1A	C3	-0,819	-0,817
HIF2/EPAS1	G1	0,655	-0,639
HIF2/EPAS1	G2	-0,192	-0,738
HIF2/EPAS1	G3	0,274	-0,820
HIF2/EPAS1	G6	-0,254	-0,744

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
HRAS	C6	0,662	-0,360
HRAS	C7	-0,654	-0,826
HRAS	C8	-0,350	-0,770
HRAS	C9	-0,073	-0,793
HRAS	C10	-0,168	-0,814
human LEF1	E6	-0,803	-0,821
human LEF1	E7	0,999	-0,242
human SOX2	E8	-0,977	-0,829
human SOX2	E9	-0,886	-0,825
IDH1	E2	1,621	-0,476
IDH1	E3	2,451	0,006
IDH1	E4	3,571	-0,258
IDH1	E5	1,568	-0,493
IDH1	E6	0,659	-0,676
IDH2	A3	-0,177	-0,829
IDH2	A4	-0,987	-0,831
IDH2	A6	-0,732	-0,830
IGF1R	D5	2,911	2,697
IGF1R	D6	1,463	0,559
IGF1R	D7	0,578	-0,744
IGF1R	D8	-0,214	-0,663
IGF1R	D9	1,923	-0,343
IKBKB	B11	-0,683	-0,698
IKBKB	B12	-0,922	-0,820
IKBKB	C1	-0,628	-0,815
IKBKB	C2	-0,420	-0,824
IKBKB	C3	-0,411	-0,798
IL17RA	C10	-0,901	-0,804
IL17RA	C11	-0,900	-0,806
IL17RA	C12	-0,514	-0,558
IL17RA	D1	0,405	-0,521
IL17RA	D2	1,072	0,934
IRF4	D1	-0,844	-0,819
IRF4	D2	0,729	-0,408
IRF4	D3	-0,624	-0,814
JAK2	F1	0,760	0,006
JAK2	F2	0,241	0,028
JAK2	F3	-1,000	-0,827
JAK2	F4	0,665	-0,639
JAK2	F5	-0,081	-0,750
JAK3	A6	0,586	-0,502
JAK3	A8	-0,738	-0,820
JAK3	A9	-0,128	-0,787
JAK3	A10	-0,651	-0,799
JUN	A7	0,585	-0,553
JUN	A8	-0,237	-0,809
JUN	A9	-0,331	-0,825

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
JUN	A10	1,218	-0,683
JUN	A11	-0,803	-0,821
KDM1A	D6	1,266	-0,460
KDM1A	D7	-0,729	-0,802
KDM1A	D8	-0,761	-0,811
KDM1A	D9	-1,033	-0,827
KDM1A	D10	-1,017	-0,817
KDR	B1	1,009	-0,802
KDR	B2	1,764	0,351
KDR	B3	-0,938	-0,809
KDR	B4	-0,761	-0,829
KIT	A11	-0,762	-0,831
KIT	B1	-0,049	-0,659
KIT	B2	1,411	-0,755
KIT	B3	0,282	-0,604
KRAS	F6	0,087	-0,740
KRAS	H3	0,154	-0,676
KRAS	H4	-0,192	-0,746
KRAS	H5	-0,016	-0,260
KRAS	H6	-0,661	-0,744
LDHA	D4	1,592	-0,008
LDHA	D5	1,286	-0,331
LDHA	D6	-0,883	-0,809
LDHA	D7	0,335	-0,447
LDHA	D8	0,155	-0,637
LTA4H	D10	1,400	-0,673
LTA4H	D11	1,088	-0,665
LTA4H	D12	-0,446	-0,774
LTA4H	E1	0,577	-0,617
LTA4H	E2	0,704	-0,141
LTC4S	E3	4,522	3,869
LTC4S	E4	1,784	-0,604
LTC4S	E5	0,448	-0,539
LTC4S	E6	0,512	-0,271
MAFF	A8	-0,714	-0,828
MAFF	A9	0,041	-0,727
MAFF	A11	0,037	-0,714
MAFF	A12	-0,967	-0,828
MAML2	G5	-0,113	-0,603
MAML2	G6	-0,045	-0,585
MAML2	G7	-0,967	-0,807
MAML2	G8	-1,003	-0,825
MAML2	G9	-0,849	-0,813
MAPK14	A3	3,587	2,330
MAPK14	A4	-0,780	-0,816
MAPK14	A5	0,292	-0,566
MAPK14	A6	-0,511	-0,807

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
MAPK14	A7	-0,616	-0,807
MAPK9	D2	0,429	-0,644
MAPK9	D3	0,374	-0,786
MAPK9	D4	1,385	-0,728
MCL1	E4	0,209	-0,669
MCL1	E5	-0,843	-0,822
MCL1	E6	-0,711	-0,809
MCL1	E7	-1,015	-0,825
MCL1	E8	-1,053	-0,822
MDM2	B5	-0,149	-0,747
MDM2	B6	-0,948	-0,830
MDM2	B7	-0,157	-0,800
MDM2	B8	2,748	0,457
MET	B4	-0,641	-0,821
MET	B5	0,676	0,424
MET	B6	0,274	-0,789
MET	B7	3,798	-0,169
MLL	F5	0,346	-0,744
MLL	F6	0,318	-0,649
MLL	F7	-0,960	-0,826
MLL	F8	-0,487	-0,797
MLL	F9	-0,675	-0,826
MLL2	G11	-0,787	-0,807
MLL2	G12	0,092	-0,814
MLL2	H1	-0,565	-0,822
MLL2	H2	0,544	-0,808
MTOR	E3	-0,634	-0,800
MTOR	E4	0,107	-0,741
MTOR	E5	-1,068	-0,831
MTOR	E6	-0,709	-0,802
MTOR	E7	-0,631	-0,826
MYC	B9	-0,520	-0,782
MYC	B10	2,104	-0,402
MYC	B11	-0,624	-0,830
MYC	C1	0,261	-0,600
NANOG	C8	-0,808	-0,816
NANOG	C9	-0,202	-0,772
NANOG	C11	0,632	-0,494
NANOG	C12	-0,650	-0,820
NFKB1	C6	-0,743	-0,824
NFKB1	C7	-0,760	-0,821
NFKB2	C2	1,284	-0,408
NFKB2	C3	-0,704	-0,814
NFKB2	C4	1,484	0,143
NFKB2	C5	1,436	-0,455
NFKB2	C6	3,496	0,241
NOTCH1	E1	0,529	-0,625

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
NOTCH1	E2	0,117	-0,782
NOTCH1	E3	-0,028	-0,209
NOTCH3	B9	-0,760	-0,688
NOTCH3	B10	0,211	-0,604
NOTCH3	B11	-0,282	-0,810
NOTCH3	B12	0,843	-0,472
NOTCH3	C1	-0,607	-0,800
NRAS	C7	-0,924	-0,812
NRAS	C8	3,575	-0,016
NRAS	C9	2,339	-0,544
NRAS	C10	2,329	1,048
NRAS	C11	-0,678	-0,818
PARP1	C4	1,068	-0,201
PARP1	C5	0,217	-0,564
PARP1	C6	0,075	-0,807
PARP1	C7	5,196	-0,235
PARP1	C8	-0,539	-0,769
PDGFR a	F8	2,917	0,236
PDGFR a	F9	-0,906	-0,806
PDGFR a	F10	-0,654	-0,780
PDGFR b	F3	-0,504	-0,812
PDGFR b	F5	3,557	0,123
PDGFR b	F6	-0,127	-0,804
PDGFR b	F7	-0,904	-0,814
PIK3CA	G7	0,580	-0,730
PIK3CA	G8	-0,679	-0,771
PIK3CA	G9	-0,276	-0,822
PIK3CA	G10	-1,077	-0,830
PIK3CA	G11	-1,065	-0,823
PLK1	F7	-0,903	-0,819
PLK1	F9	-0,700	-0,801
PLK1	F10	-0,916	-0,827
PLK1	F11	-0,866	-0,827
POU5F1B	F5	4,981	1,310
POU5F1B	F6	-0,860	-0,783
POU5F1B	F8	-0,656	-0,780
POU5F1B	F9	-0,550	-0,749
PPARGC1A	C5	-0,906	-0,816
PPARGC1A	C6	0,354	-0,729
PPARGC1A	C7	-0,912	-0,817
PPARGC1A	C8	-0,901	-0,816
PPARGC1A	C9	-0,905	-0,823
PTGER2	E7	9,196	7,018
PTGER2	E8	0,994	-0,156
PTGER2	E9	-0,287	-0,673
PTGER2	E10	-0,140	-0,791
PTGER2	E11	-0,819	-0,815

Table S6

GENE_SYMBOL	ShRNA_ID	Z_D3	Z_D7
PTGES	D10	-0,809	-0,825
PTGES	D11	-0,878	-0,824
PTGES	E1	-1,076	-0,817
PTGES	E2	0,617	-0,132
PTK2	D9	-0,875	-0,821
PTK2	D10	-1,053	-0,826
PTK2	D11	-1,047	-0,815
PTK2	E1	2,536	0,468
RAC1	A3	-0,120	-0,755
RAC1	A4	-0,272	-0,827
RAC1	A5	-0,798	-0,830
RAC1	A6	-0,945	-0,826
RAC1	A7	-0,661	-0,814
RAC2	D6	2,649	0,300
RAC2	D7	3,173	-0,091
RAC2	D8	0,489	-0,263
RAC2	D9	-0,133	-0,824
RAC3	G1	-0,562	-0,692
RAC3	G2	-0,023	-0,733
RAC3	G3	-0,189	-0,649
RAC3	G4	-0,341	-0,769
RAF1	D10	0,772	-0,591
RAF1	D11	-0,861	-0,822
RAF1	D12	-0,629	-0,818
RAF1	E1	-0,841	-0,831
RAF1	E2	-0,718	-0,825
REL	E3	-0,972	-0,830
REL	E4	-0,743	-0,827
REL	E7	0,159	-0,674
RELA	E9	-1,057	-0,824
RELA	E10	-0,924	-0,813
RELA	E11	-0,996	-0,803
RELA	F1	0,741	-0,068
RELB	H1	-0,019	-0,783
RELB	H2	0,302	-0,564
RELB	H3	0,150	-0,565
RELB	H4	-0,451	-0,817
RELB	H5	-0,546	-0,793
RHO	C7	2,670	-0,299
RHO	C8	-0,921	-0,825
RHO	C9	2,047	0,349
RHO	C10	2,773	0,398
RHO	C11	-0,994	-0,822
ROS1	E8	2,024	0,246
ROS1	E9	-0,753	-0,823
ROS1	E10	-0,541	-0,810
ROS1	E11	-0,825	-0,817

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
RPS6	E12	-0,733	-0,824
RPS6	F2	-0,839	-0,814
RPS6	F3	0,123	-0,800
RUNX1	D7	0,374	-0,613
RUNX1	D8	-0,546	-0,787
RUNX1	D9	-0,806	-0,803
RUNX1	D10	-0,443	-0,720
RUNX1	D11	-0,724	-0,817
RUNX2	B9	-0,168	-0,813
SGK	B4	-0,837	-0,825
SGK	B5	5,143	-0,819
SGK	B6	0,439	0,049
SGK	B7	-0,492	-0,815
SIRT1	B7	-0,918	-0,738
SIRT1	B8	-1,010	-0,819
SIRT1	B10	-1,025	-0,824
SIRT1	B11	-0,962	-0,817
SKP2	F10	-0,759	-0,744
SKP2	G1	1,770	0,869
SLC2A1	H6	-0,697	-0,790
SLC2A1	H7	0,068	-0,720
SLC2A1	H8	-0,111	-0,464
SLC2A1	H9	-0,776	-0,820
SLC2A1	H10	-0,683	-0,824
SMAD2	E7	0,467	-0,790
SMAD2	E8	-0,786	-0,775
SMAD2	E9	-0,603	-0,819
SMAD2	E10	-0,829	-0,826
SMAD2	E11	-0,820	-0,779
SMAD3	F1	0,213	-0,559
SMAD3	F2	0,886	-0,331
SMAD3	F3	0,376	-0,656
SMAD3	F4	-0,003	-0,694
SMAD4	D1	2,006	0,203
SMAD4	D2	1,062	-0,561
SMAD4	D3	0,664	-0,755
SMO	D9	0,438	-0,617
SMO	D10	-0,035	-0,799
SMO	D11	-0,137	-0,746
SMO	D12	-0,772	-0,809
SMO	E1	-0,625	-0,821
SNAI2	F1	-1,077	-0,831
SNAI2	F3	-0,527	-0,792
SNAI2	F4	0,364	-0,176
SNAI2	F5	-0,436	-0,785
SNFT	G7	-0,581	-0,807
SNFT	G8	-0,171	-0,795

Table S6

GENE_SYMBOL	SHRNA_ID	Z_D3	Z_D7
SNFT	G9	-0,224	-0,446
SRCIN1	F7	-0,841	-0,823
SRCIN1	F8	-0,551	-0,768
SRCIN1	F9	-1,031	-0,824
SRCIN1	F10	-0,935	-0,818
STAT1	A9	-0,980	-0,816
STAT1	A10	-0,971	-0,813
STAT1	A11	-0,498	-0,806
STAT1	B1	-0,834	-0,797
STAT3	B8	-0,347	-0,803
STAT3	B9	-1,068	-0,833
STAT5A	F6	3,499	-0,205
STAT5A	F7	-0,303	-0,716
STAT5A	F8	1,710	0,445
STAT5A	F9	1,201	-0,461
STAT5A	F10	-0,454	-0,815
STAT5B	B12	-0,946	-0,754
STAT5B	C1	-0,152	-0,692
STAT5B	C2	-0,803	-0,800
STAT5B	C3	0,147	-0,254
STAT5B	C4	0,257	-0,674
TCF4	F11	0,744	-0,566
TCF4	F12	-0,255	-0,811
TCF4	G1	0,120	-0,772
TCF4	G2	1,001	-0,693
TCF4	G3	-0,531	-0,765
TERT	G4	-0,257	-0,651
TERT	G5	-0,937	-0,825
TNS4	G10	-0,920	-0,822
TNS4	G12	-0,919	-0,799
TNS4	H1	-0,594	-0,724
TNS4	H2	0,007	-0,652
TRAF6	D1	0,323	-0,567
TRAF6	D2	0,523	-0,519
TRAF6	D3	0,494	-0,620
TRAF6	D4	-0,946	-0,814
TWIST1	C2	2,085	0,787
TWIST1	C3	0,108	-0,537
TWIST1	C4	-0,546	-0,732
TWIST1	C5	-0,510	-0,734
TWIST1	C6	2,097	0,573
UBE2D2	G6	-1,064	-0,830
UBE2D2	G7	3,911	-0,115
UBE2D2	G9	0,111	-0,689
UBE2D2	G10	1,334	-0,760
XIAP	G8	-0,591	-0,645
XIAP	G9	0,722	-0,555

Table S6

GENE_SYMBOL	ShRNA_ID	Z_D3	Z_D7
XIAP	G11	-0,990	-0,831
XIAP	G12	-0,804	-0,784
ZEB1	F12	-0,864	-0,762
ZEB1	G1	-0,695	-0,773
ZEB1	G2	-0,294	-0,211
ZEB1	G3	-0,622	-0,683
ZEB1	G4	-0,124	-0,758

Table S7

GENE_SYMBOL
ABL2
AKT1
AKT2
ATF1
CCND1
CDK4
CDK7
EZH2
FLT4
IDH2
KDM1A
MAML2
MCL1
PLK1
PPARGC1A
PTGES
PTK2
REL
RELA
SIRT1
SMAD2
SOX2
SRCIN1
STAT1