

The high NRF2 expression confers chemotherapy resistance partly through up-regulated DUSP1 in myelodysplastic syndromes

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Received: May 15, 2018.

Accepted: September 26, 2018.

Pre-published: September 27, 2018.

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Title: The high NRF2 expression confers chemotherapy resistance partly through up-regulated DUSP1 in myelodysplastic syndromes

Running title: NRF2 and Ara-C resistance in MDS

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Conflicts of Interest: The authors declare that they have no relevant conflicts of interest.

Supplementary information

- Supplementary Figure S1-S8 and Supplementary Figure Legends;
- Supplementary Table S1-S6;
- Supplementary Methods;
- Supplemental List 1-3

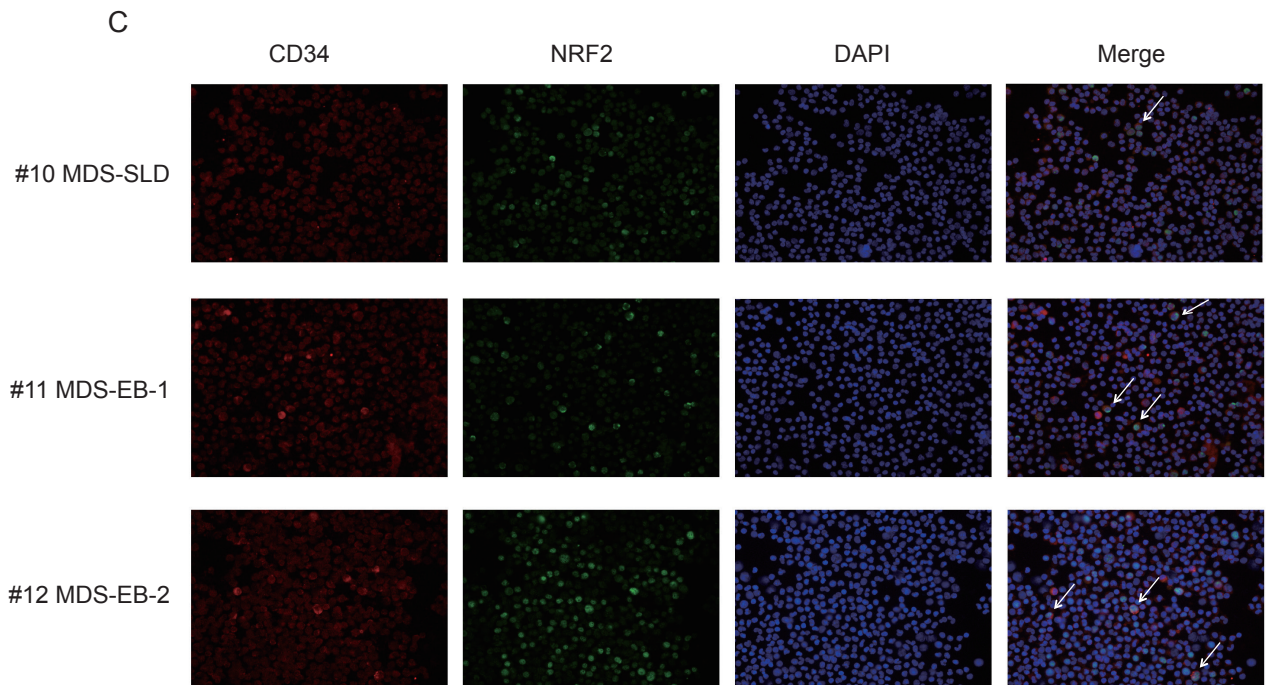
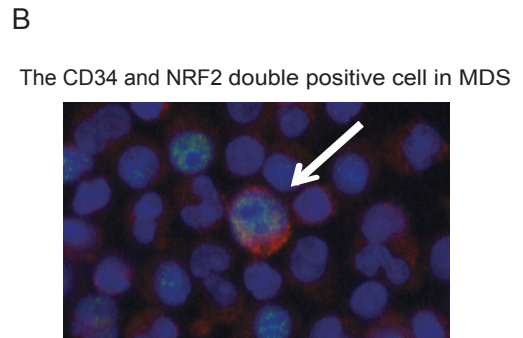
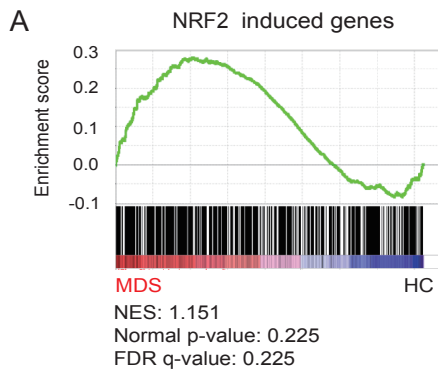


Figure S1. (A) Gene set enrichment plot of NRF2 target genes in MDS patients and healthy controls (HC). (B) CD34 (red) and NRF2 (green) double-immunofluorescence staining in MDS. (C) Immunofluorescence results of CD34 (red), NRF2 (green) and DAPI (blue) staining in MDS patient samples (magnification $\times 400$).

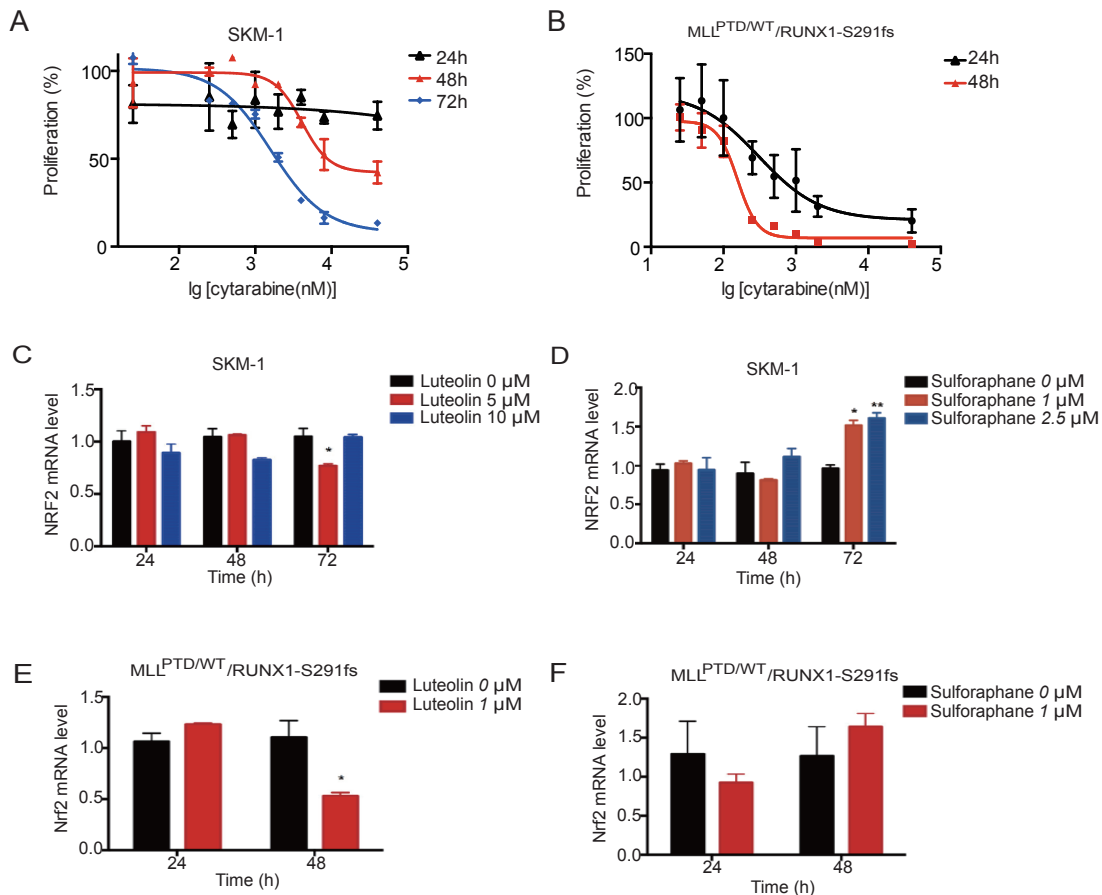


Figure S2. Effects of Ara-C on proliferations of (A) SKM-1 and (B) MLL^{PTD/WT}/RUNX1-S291fs cells lines. NRF2 mRNA levels of SKM-1 cells treated with (C) Luteolin and (D) Sulforaphane. Nrf2 mRNA levels of MLL^{PTD/WT}/RUNX1-S291fs cells treated with (E) Luteolin and (F) Sulforaphane.

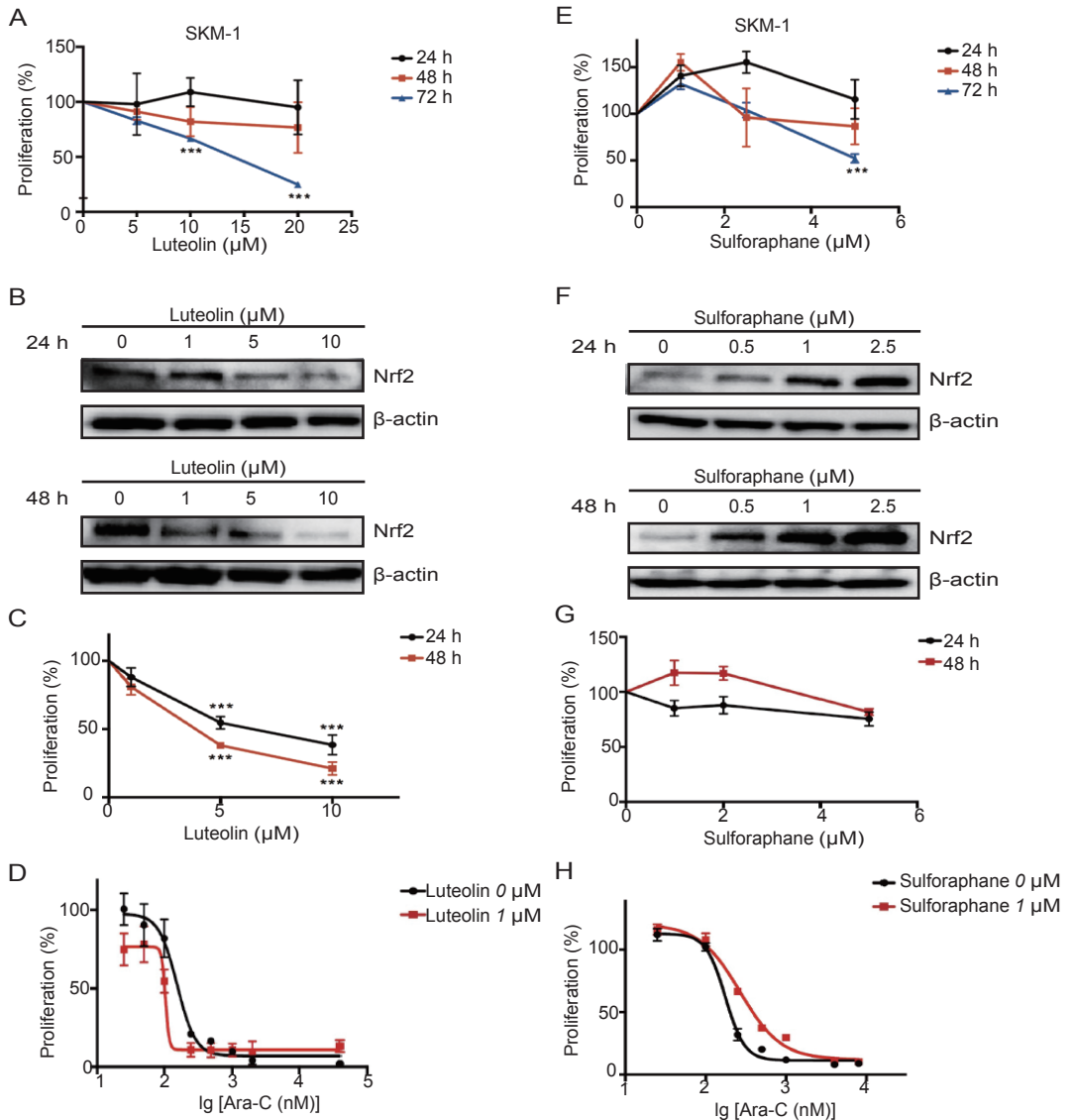


Figure S3. (A) Lower concentrations of Luteolin had little effect on cell proliferation in SKM-1. (B) Luteolin decreased NRF2 protein levels in MLL^{PTD/WT}/RUNX1-S291fs. (C) Lower concentrations of Luteolin had little effect on cell proliferation in MLL^{PTD/WT}/RUNX1-S291fs. (D) Ara-C IC50 was significantly decreased by Luteolin in MLL^{PTD/WT}/RUNX1-S291fs. (E) Lower concentrations of Sulforaphane had little effect on the proliferation in SKM-1. (F) Sulforaphane increased NRF2 protein levels in MLL^{PTD/WT}/RUNX1-S291fs. (G) Lower concentrations of Sulforaphane had little effect on the proliferation in MLL^{PTD/WT}/RUNX1-S291fs. (H) Ara-C IC50 was significantly increased by Sulforaphane treatment in MLL^{PTD/WT}/RUNX1-S291fs.

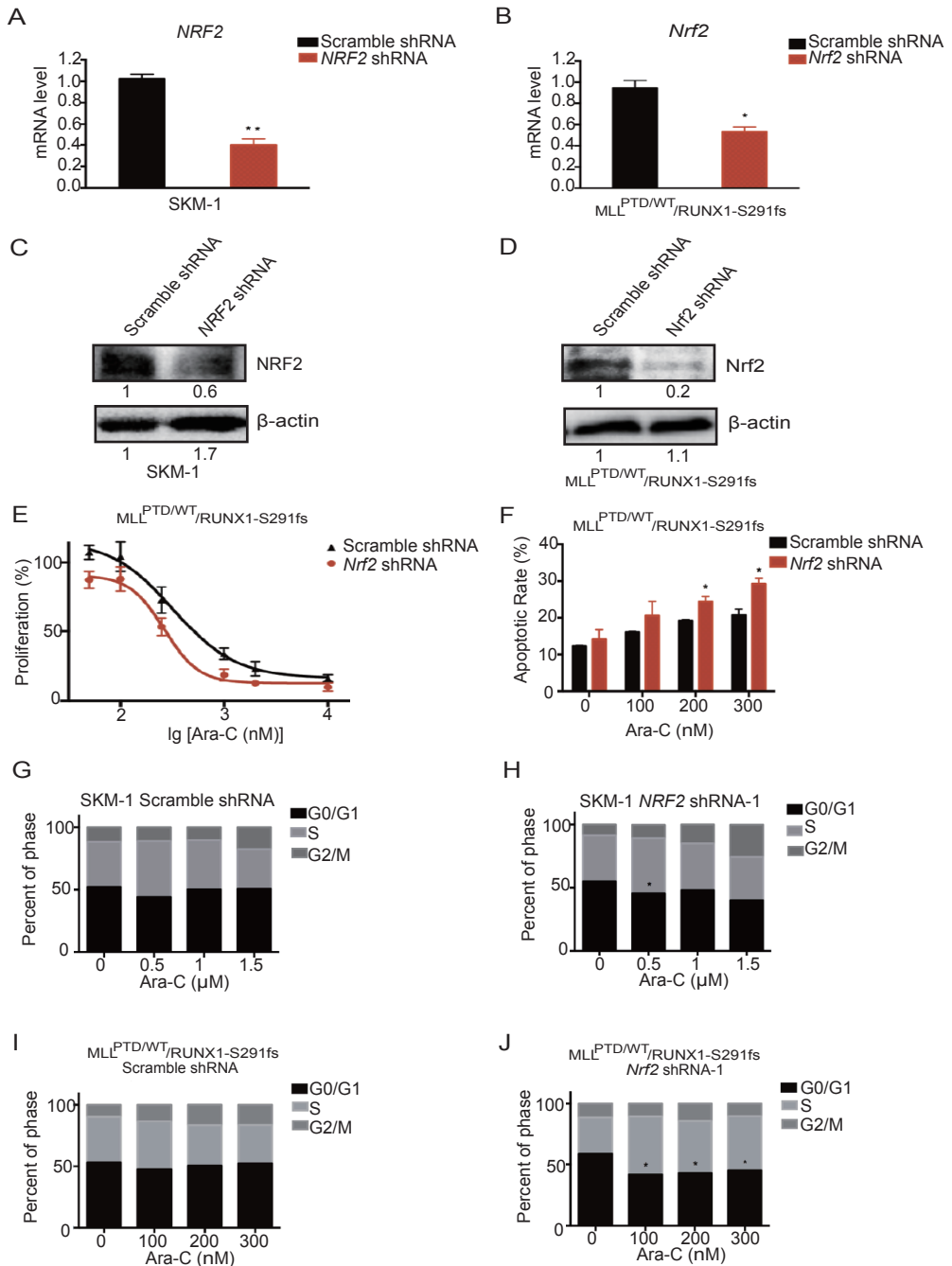


Figure S4. NRF2 shRNA repressed NRF2 mRNA levels in (A) SKM-1 cells and (B) MLL^{PTD/WT}/RUNX1-S291fs. NRF2 shRNA repressed NRF2 protein levels in (C) SKM-1 cells and (D) MLL^{PTD/WT}/RUNX1-S291fs. (E) NRF2 silencing significantly decreased IC₅₀ of Ara-C in MLL^{PTD/WT}/RUNX1-S291fs. (F) NRF2 shRNA enhanced apoptosis induced by Ara-C in MLL^{PTD/WT}/RUNX1-S291fs. (G-J) NRF2 shRNA induced S phase arrest in SKM-1 and MLL^{PTD/WT}/RUNX1-S291fs treated by Ara-C.

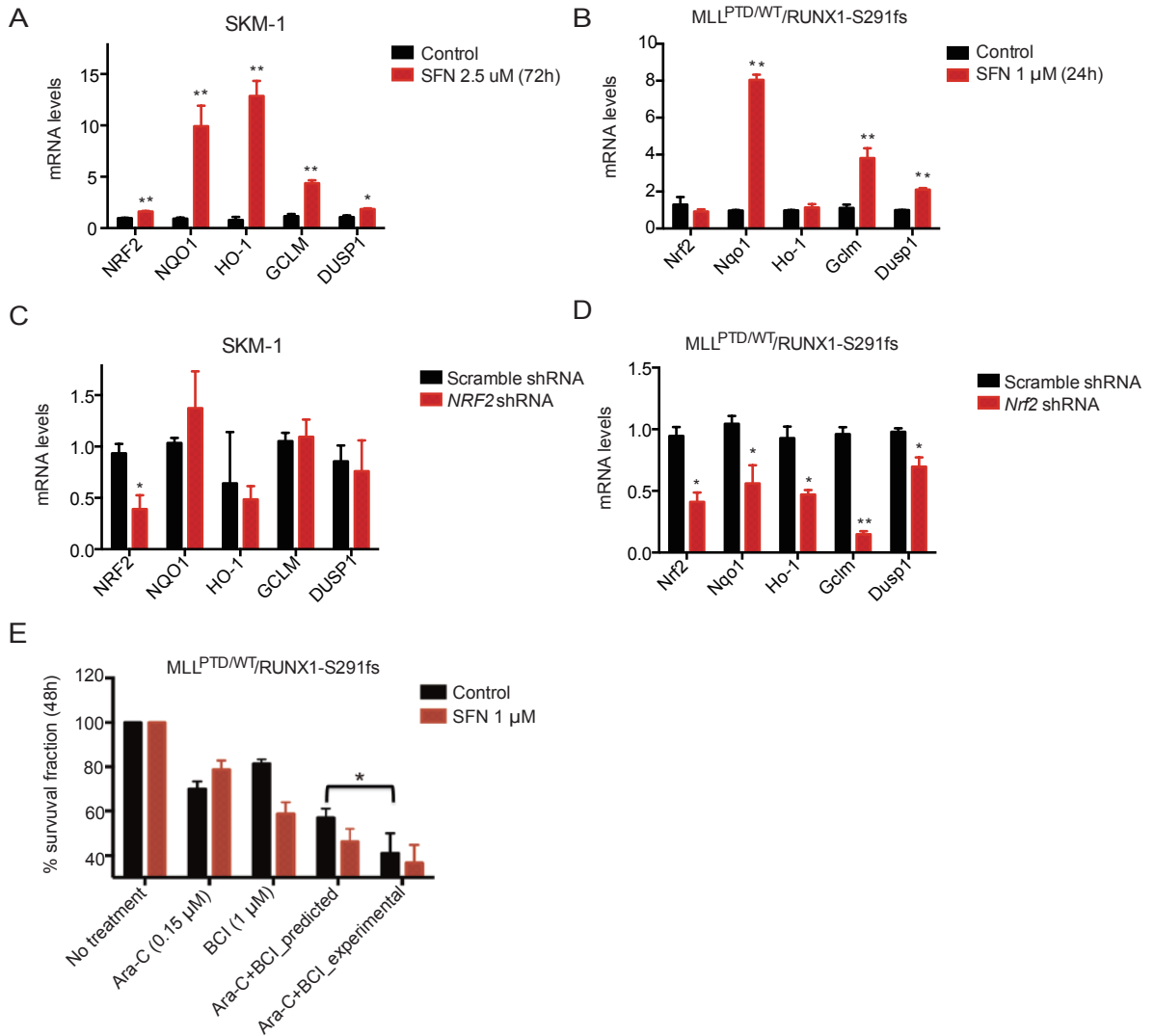


Figure S5. DUSP1 was overexpressed in SFN treated (A) SKM-1 and (B) MLL^{PTD/WT}/RUNX1-S291fs cells lines. (C) No significant changes in NRF2 target genes in NRF2 shRNA SKM-1 cells. (D) DUSP1 was downregulated in Nrf2 shRNA MLL^{PTD/WT}/RUNX1-S291fs cells lines. (E) Ara-C and BCI have synergistic effects in MLL^{PTD/WT}/RUNX1-S291fs cells lines.

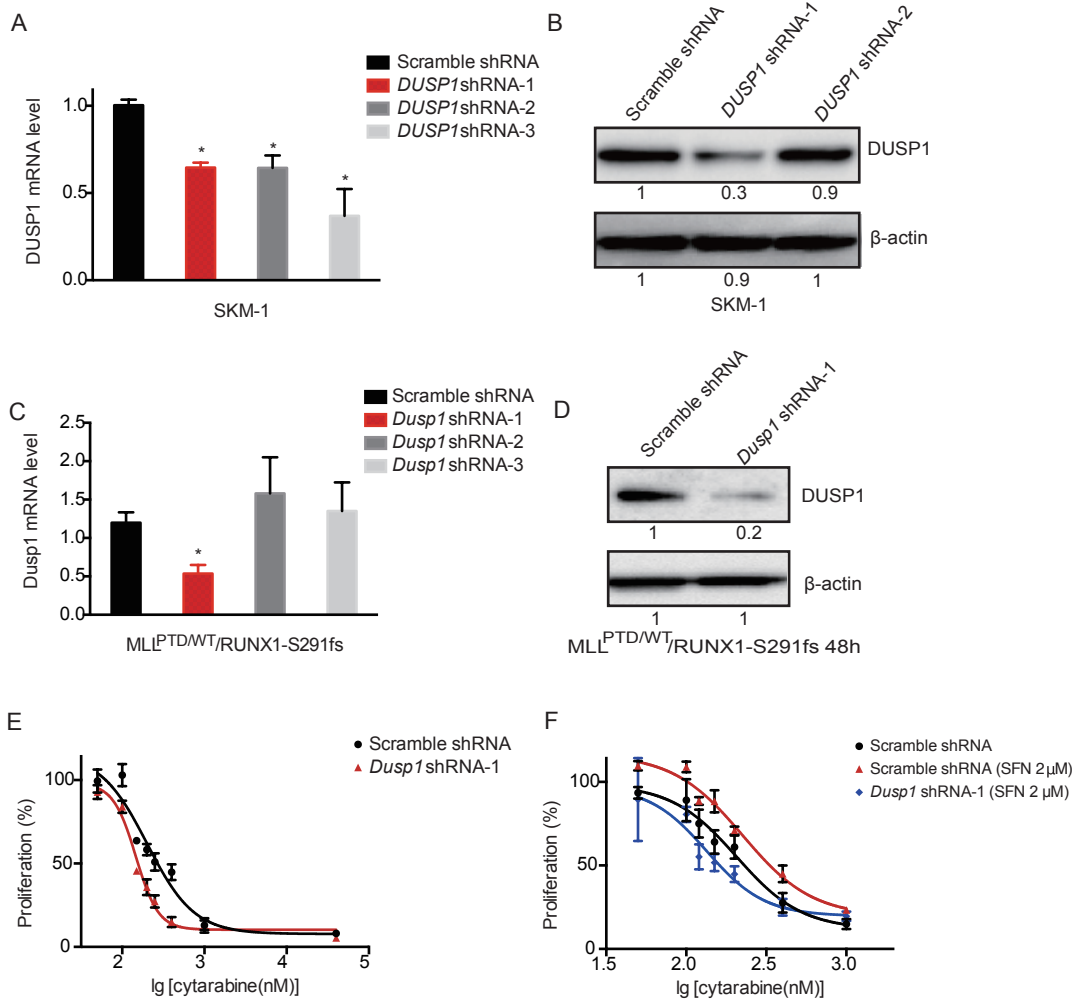
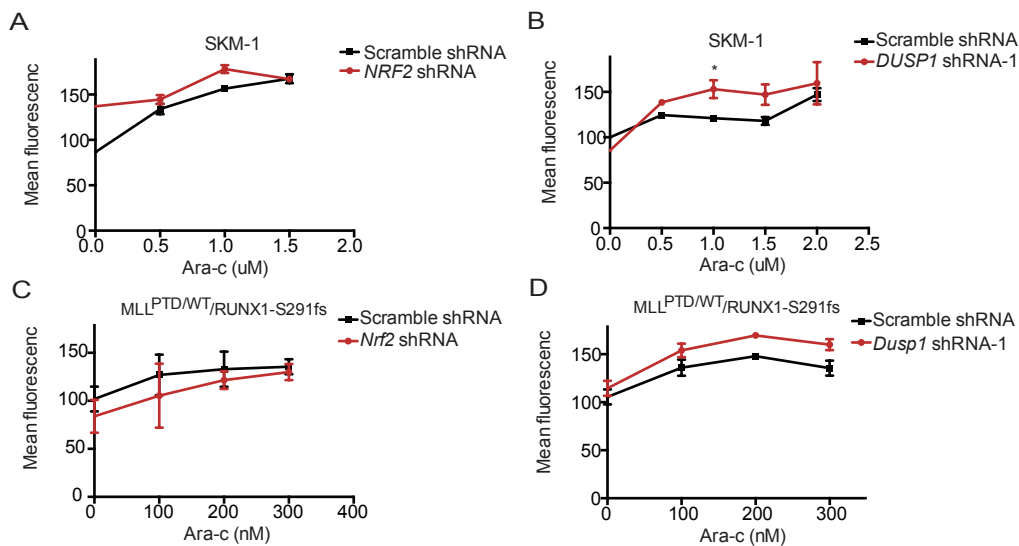


Figure S6. *DUSP1* shRNA-1 repressed *DUSP1* (A) mRNA and (B) protein levels in SKM-1. *Dusp1* shRNA-1 repressed *Dusp1* (C) mRNA and (D) protein levels in MLL^PT^D/WT/RUNX1-S291fs cells lines. (E) *Dusp1* silencing significantly decreased IC₅₀ of Ara-C in MLL^PT^D/WT/RUNX1-S291fs cells lines. (F) *Dusp1* shRNA-1 re-sensitized NRF2 agonist treated MLL^PT^D/WT/RUNX1-S291fs cells to Ara-C.



E Up-regulated genes in higher risk MDS
FC>1.1, rawp <0.05
Total 5477 genes

Up-regulated genes in Ara-C resistant AML
FC>1.1, rawp <0.05
Total 3074 genes



KEGG pathway analysis

F

No.	Term	Genes	Count	P-Value	Benjamini
1	MAPK signaling pathway	MKNK1, RAPGEF2, TNFRSF1A, ARRB2, DUSP1, DUSP6, HSPA1L, MAPK14, MAP3K12, PAK1, PPM1B, RAC2, RRAS, ZAK	14	0.0014	0.2300
2	Chemokine signaling pathway	CXCL6, GNB1, JAK2, ARRB2, DOCK2, FOXO3, PAK1, PXN, PRKCZ, RAC2, STAT2	11	0.0034	0.2700
3	Apoptosis	ATM, CFLAR, TNFRSF10C, TNFRSF10D, TNFRSF1A, APAF1	6	0.0070	0.3600
4	Jak-STAT signaling pathway	JAK2, CSF3R, CCND3, IFNGR1, IL10RB, IL6R, PIAS1, STAT2, TSLP	9	0.0073	0.2900
5	FoxO signaling pathway	ATM, GABARAPL1, RBL2, CCNG2, FOXO3, HOMER1, IGF1R, MAPK14	8	0.0160	0.4500
6	Influenza A	JAK2, TNFRSF10C, TNFRSF10D, TNFRSF1A, CASP1, HSPA1L, IFNGR1, MAPK14, STAT2	9	0.0200	0.4700
7	Legionellosis	NAIP, APAF1, CASP1, EEF1A1, HSPA1L	5	0.0210	0.4300
8	NOD-like receptor signaling pathway	NAIP, CASP1, CARD6, MAPK14, PSTPIP1	5	0.0220	0.4100
9	Sphingolipid signaling pathway	ASAH1, TNFRSF1A, MAPK14, PRKCZ, PPP2R5A, RAC2, SGPL1	7	0.0300	0.4700
10	Lysosome	ASAH1, CLN5, HGSNAT, LAPTM5, MFSD8, SCARB2, TPP1	7	0.0310	0.4400
11	Phosphatidylinositol signaling system	DGKZ, INPP4A, INPP5A, MTMR3, SYNJ1, TMEM55A	6	0.0420	0.5200
12	Measles	JAK2, TNFRSF10C, TNFRSF10D, CCND3, HSPA1L, IFNGR1, STAT2	7	0.0450	0.5200

Figure S7. ROS levels in (A) NRF2 shRNA and (B) DUSP1 shRNA SKM-1 cells. ROS levels in (C) NRF2 shRNA and (D) DUSP1 shRNA MLL^{PTD/WT}/RUNX1-S291fs cells. (E) Overlap of up-regulated NRF2 target genes in higher-risk MDS patients and Ara-C resistant AML patients (Fold change >1.1, rawp <0.05). (F) Enriched KEGG pathways of 331 overlapped common genes.

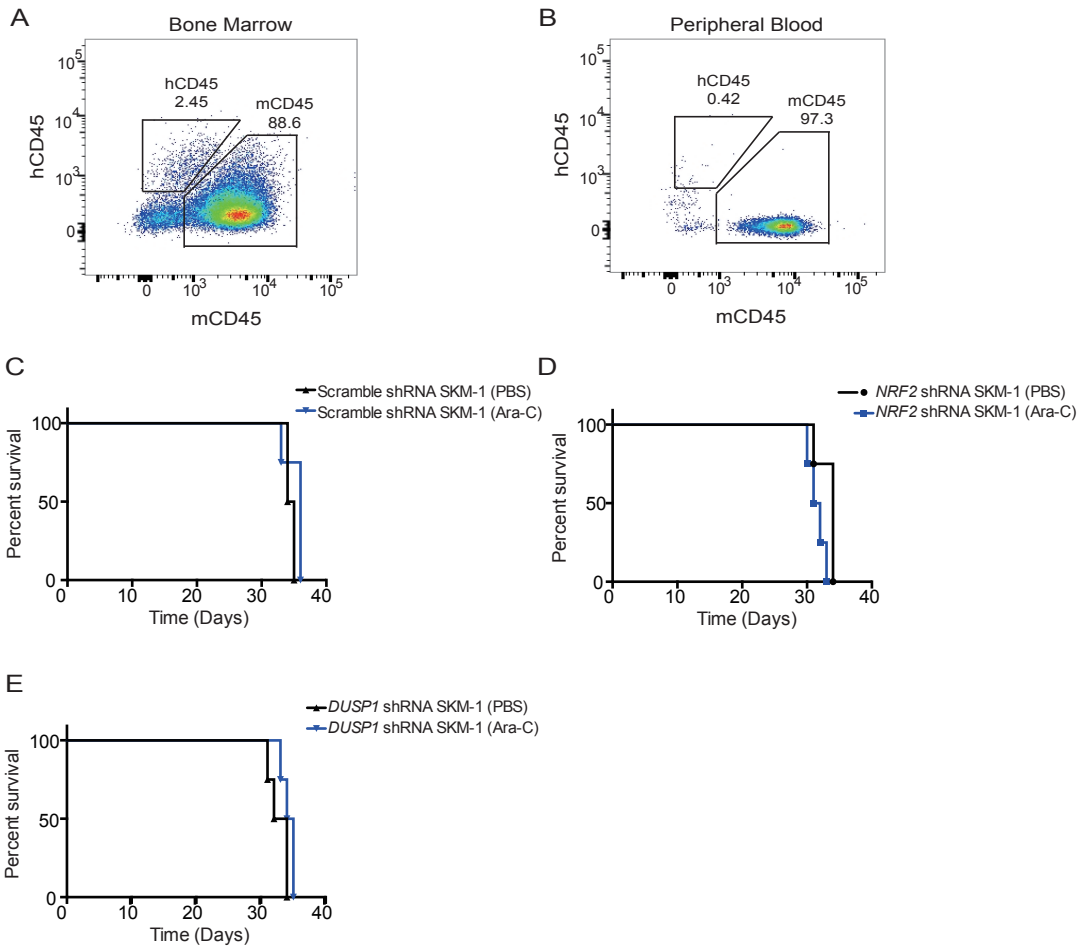


Figure S8. Flow cytometry analysis of human CD45⁺ cells and mouse CD45⁺ cells in **(A)** bone marrow and **(B)** peripheral blood of NSGS mice. Survival curves of **(C)** scramble shRNA, **(D)** NRF2 knockdown and **(E)** DUSP1 knockdown SKM-1 transplanted mice.

Supplemental Tables

Table S1. Comparison of NRF2 expression between lower risk and higher risk MDS patients

	NRF2 IHC scores 0-1	NRF2 IHC scores 2-6	χ^2	P value
Lower risk groups	12	17	8.163	0.004
Higher risk groups	18	90		

Lower risk groups: MDS patients with low risk (IPSS-R scores >1.5~3); Higher risk groups: MDS patients with intermediate, high and very high risk (IPSS-R scores >3).

Table S2. Clinical and molecular characteristics of 137 MDS patients enrolled in immunohistochemical research.

Variable	Total	NRF2 IHC scores 0-3	NRF2 IHC scores 4-6	P value
Patients, n (%)	137	122 (89.1)	15 (10.9)	
Age, median (range)	58 (18-87)	58 (18-87)	59 (33-70)	0.70
Male, n (%)	85 (62.0)	75 (61.5)	10 (66.7)	0.70
MDS Subtype, n (%)				0.022
MDS-SLD	15 (10.9)	15 (12.3)	0 (0)	
MDS-RS	9 (6.6)	9 (7.4)	0 (0)	
MDS-MLD	40 (29.2)	38 (31.1)	2 (13.3)	
MDS-EB-1	38 (27.7)	30 (24.6)	8 (53.3)	
MDS-EB-2	35 (25.6)	30 (24.6)	5 (33.4)	
Hemoglobin (g/L), median (range)	79 (34-158)	80 (34-158)	71 (52-94)	0.22
WBC ($\times 10^9/L$), median (range)	4.4 (0.6–37.4)	4.4 (0.6-37.4)	4.2 (0.6-15.3)	0.89
Platelets ($\times 10^9/L$), median (range)	96 (4–509)	101 (4-509)	60 (5-175)	0.13
Blasts (%), median (range)	6.4 (0-18.5)	6.2 (0-18.5)	7.8 (0-18.0)	0.26
Transformation, n (%)				0.95
AML transformation	118 (86.1)	105 (86.1)	13 (86.7)	
Non- transformation	19 (13.9)	17 (13.9)	2 (13.3)	
IPSS cytogenetics, n (%)				0.001
Low risk	94 (68.6)	89 (73.0)	5 (33.3)	
Intermediate risk	15 (10.9)	13 (10.7)	2 (13.3)	
High risk	28 (20.5)	20 (16.3)	8 (53.4)	
IPSS categories, n (%)				0.001
Low risk	18 (13.1)	18 (14.8)	0 (0)	
Intermediate-1 risk	60 (43.8)	56 (45.9)	4 (26.7)	
Intermediate-2 risk	35 (25.5)	32 (26.2)	3 (20.0)	
High risk	24 (17.6)	16 (13.1)	8 (53.3)	
Treatment, n (%)				0.84
Chemotherapy	30 (21.9)	27 (22.1)	3 (20.0)	
Decitabine	28 (19.2)	25 (20.5)	3 (20.0)	
Supportive care	79 (57.7)	70 (57.4)	9 (60.0)	
Overall Survival, median (days)	526	554	391	0.01

Abbreviations: WBC, white blood cell count; ANC, absolute neutrophil count; IPSS categories scores: Low risk, 0; intermediate-1, 0.5–1; Intermediate-2, 1.5–2; and high risk, ≥ 2.5 .

Table S3 Primary MDS cells information

Number	Age, y	Sex	WHO diagnosis	% blasts	Cytogenetics
MDS #1	59	Male	MDS-EB-2	17%	46, XY [20]
MDS #2	52	Male	MDS-EB-2	4%	46, XY [20]
MDS #3	56	Female	MDS-EB-2	19%	47, XX, +8 [10]
MDS #4	69	Female	MDS-SLD	4.5%	46, XX, +8 [3]
MDS #5	52	Male	MDS-EB-1	5%	47, XY, +8 [10]
MDS #6	70	Female	MDS-EB-1	5%	46, XX, der(5)(q32) [16]
MDS #7	40	Female	MDS-EB-2	16%	47, XY, +18 [1]
MDS #8	47	Male	MDS-EB-1	8.5%	46, XY [20]
MDS #9	57	Male	MDS-MLD	4.5%	47, XY, +8 [10]
MDS #10	61	Male	MDS-SLD	1%	46, XY [20]
MDS #11	62	Male	MDS-EB-1	5.5%	46, XY [20]
MDS #12	56	Male	MDS-EB-2	10%	46, XY [20]

Table S4 ShRNA clones

Vector Name	Ref Seq No	TRCN
<i>NRF2</i> shRNA	NM_006164.2	7557
<i>Nrf2</i> shRNA	NM_010902.2	12130
<i>DUSP1</i> shRNA-1	NM_004417	2514
<i>DUSP1</i> shRNA-2	NM_004417	2515
<i>DUSP1</i> shRNA-3	NM_004417	2517
<i>Dusp1</i> shRNA-1	NM_013642	54678
<i>Dusp1</i> shRNA-2	NM_013642	54679
<i>Dusp1</i> shRNA-3	NM_013642	54680

Table S5 Primer sequences for ChIP q-PCR

Genes	Forward Primer	Reverse Primer
<i>NQO1</i>	GCAGTCACAGTGACTCAGC	TGTGCCCTGAGGTGCAA
<i>DUSP1</i>	TGGATACTGTTCATGGAGG	GCTCACAAAGTTGAATTGAC
Negative	GGATTTCCACTTAGCAGATA	GGCAACATTCCTGTAAAAT

Table S6 Primer sequences for q-PCR analysis

Genes	Forward Primer	Reverse Primer
<i>NRF2</i>	TCAGCGACGGAAAGAGTATGA	CCACTGGTTTCTGACTGGATGT
<i>DUSP1</i>	CTGCCTTGATCAACGTCTCA	ACCCTTCCTCCAGCATTCTT
<i>NQO1</i>	GAAGAGCACTGATCGTACTGGC	GGATACTGAAAGTTCGCAGGG
<i>GCLM</i>	TGTCTTGGAATGCACTGTATCTC	CCCAGTAAGGCTGTAAATGCTC
<i>HO-1</i>	TTGCCAGTGCCACCAAGTTC	TCAGCAGCTCCTGCAACTCC

<i>GAPDH</i>	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG
<i>Nrf2</i>	CTTTAGTCAGCGACAGAAGGAC	AGGCATCTTGTTTGGGAATGTG
<i>Dusp1</i>	GTTGTTGGATTGTCGCTCCTT	TTGGGCACGATATGCTCCAG
<i>Nqo1</i>	AGGATGGGAGGTACTCGAATC	AGGCGTCCTTCCTTATATGCTA
<i>Gclm</i>	AGGAGCTTCGGGACTGTATCC	GGGACATGGTGCATTCCAAAA
<i>Ho-1</i>	AGGATGGGAGGTACTCGAATC	AGGCGTCCTTCCTTATATGCTA
<i>Gapdh</i>	AGGTCGGTGTGAACGGATTTG	TGTAGACCATGTAGTTGAGGTCA

Supplemental Methods

Patient cohort for IHC

From May 2010 to July 2017, 137 MDS patients at the First Affiliated Hospital of Zhejiang University were included in this study after obtaining informed consent in accordance with the Declaration of Helsinki. Bone marrow (BM) specimens were obtained by biopsy at the time of diagnosis. Patients were treated with chemotherapy including GAA regimen (granulocyte-colony stimulating factor [G-CSF] 200 $\mu\text{g}/\text{m}^2$, days 1–14; aclacinomycin 10 mg/day, days 1–14; cytarabine 10 mg/m^2 , days 1–14), and AA regimen (aclacinomycin 10 mg/day, days 1–14; cytarabine 10 mg/m^2 , days 1–14); the hypomethylating agent decitabine (20 $\text{mg}/\text{m}^2/\text{d}$, days 1–5); or supportive care such as growth factor support using G-CSF and erythroid-stimulating agents (ESAs), blood transfusion, iron chelation therapy.

Immunofluorescence

Cells were fixed with 4% paraformaldehyde and permeabilized with 0.1% Triton X-100, followed by 3%BSA blocking before primary and secondary antibody incubation. The dilution factors for each primary antibody are as follows, anti-CD34 (dilution 1:100; abcam,

UK) and anti-NRF2 (dilution 1:100; abcam, UK). Alexa Fluor 488 conjugated goat anti-rabbit IgG (dilution 1:400; Servicebio, Carlsbad, China) and Cy3 conjugated goat anti-mouse IgG (dilution 1:300; Servicebio, Carlsbad, China) were used as secondary antibodies. Then cells were incubated with DAPI (Servicebio, Carlsbad, China) at room temperature for 10 min. Imaging was performed using Nikon DS-U3 imaging system.

Gene expression profiling analysis

RNA from bone marrow cells was previously profiled on microarrays (GSE19429, GSE33787).^{[1],[2]} Gene set enrichment analysis (GSEA) was used to determine whether the transcriptional signature produced by NRF2 was significantly related to MDS categories or Ara-C resistance in AML patients. According to the French–American–British (FAB) criteria, MDS patients subdivided into refractory anaemia (RA) (n=55), refractory anaemia with ring sideroblasts (RARS) (n=48), and refractory anaemia with excess blast type-1 (RAEB-1) (n=37) and RAEB-2 (n=43). AML patients subdivided into the Ara-C sensitive (Ara-C IC50 <6 μ M, n=5) and resistant (Ara-C IC50 >80 μ M, n=5) groups. NRF2 target gene sets database was previously defined as 654 overlap genes between CHIP-Seq and basal NRF2

target dataset (genes downregulated in *Nrf2*^{-/-} versus WT mouse embryonic fibroblasts comparison).^[3] 9 of 37 overlapped up-regulated NRF2 target genes (both in higher risk MDS and Ara-C resistant AML) were reported to be associated with chemoresistance.^[4-12] KEGG pathway enrichment analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID).

Reagents and cell culture

Ara-C (Mylan, USA) were dissolved in phosphate buffer saline (PBS) and stored at 4°C. The NRF2 inhibitor Luteolin and activator Sulforaphane were purchased from Sigma (USA). (E)-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1H-inden-1-one (BCI) was kindly provided by Dr. Mohammad Azam (Cincinnati children's hospital medical center, USA).

SKM-1 cells were cultured in PRIM 1640 supplemented with 5% fetal bovine serum (FBS) and 1% penicillin/ streptomycin. *MLL*^{PTD/WT} /*RUNX1*-S291fs were cultured in Iscove's Modified Dulbecco's Medium (IMDM) supplemented with 10% FBS, 1% antibiotics and 10 nanogram/ milliliter (ng/ml) growth factors (Interleukin-3, Interleukin-6, Granulocyte-macrophage colony-stimulating factor and colony-stimulating factor).

HEK293T cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% FBS and 1% antibiotics.

Primary MDS cells were obtained under ethical approval of Zhejiang University. All patients signed informed consents for sample collections in accordance with the Declaration of Helsinki. MDS mononuclear cells from bone marrow aspirates were obtained at diagnosis (Table S3). Primary MDS cells were cultured in PRIM 1640 supplemented with 5% fetal bovine serum (FBS) and 1% penicillin/ streptomycin. Cells were plated at a density of 1×10^6 cells/ml in the medium before treatments.

Generation of stable transformant cell lines

For down-regulation of *NRF2/Nrf2* or *DUSP1/Dusp1*, HEK293T cells were transfected with lentivirus vectors for expression of pLKO.1-scramble shRNA, *NRF2/Nrf2* shRNA or *DUSP1/Dusp1* shRNA (Table S4). At 48 hours (h) post-transfection, medium was harvest and used to infect cell lines in presence of 6 microgram/ millilitre ($\mu\text{g/ml}$) polybrene. Stable cell lines were then selected using puromycin (SKM-1, $2.5\mu\text{g/ml}$; MLL^{PTD/WT}/RUNX1-S291fs, $1\mu\text{g/ml}$) for 7 days.

Flow cytometric analysis

Flow cytometric (FCM) analysis on FACSCanto Instruments was used to determine cell death by apoptosis and evaluate the cell cycle phase. For apoptosis assay, the cells were washed twice with PBS and suspended in 100 μ l binding buffer (10^6 cells/ml) with 5 μ l Annexin V (BD Biosciences, USA) and 5 μ l 7-AAD (BD Biosciences, USA) for 15 min at RT in the dark before analysis. For cell cycle analysis, the cells were fixed in 70% ice-cold ethanol overnight at -20°C . The fixed cells were washed with PBS twice and re-suspended with 100 μ l PBS containing 50 $\mu\text{g/ml}$ propidium iodide (BioLegend, USA) and 0.5 $\mu\text{g/ml}$ RNase A (Epicentre, USA). After incubation for 30 min at RT, the stained cells were analysed. The ROS levels of cells was determined by incubating the cells with 2'-7'-Dichlorodihydrofluorescein diacetate DCFDA (5 μM) (Sigma-Aldrich, USA) for 15 min followed by measuring the mean fluorescent intensity (MFI).

FCM was performed to detect the ratio of human CD45 positive cells in mouse liver tumors.

Tumor cells were incubated with 0.3 μ l anti-human CD45 (BD Bioscience, USA) and 0.3 μ l anti-mouse CD45 (BD Bioscience, USA) in 100 μ l PBS. Cells were incubated for 1 hour at

RT before analysis.

Western blotting

10⁶ cells were lysed in 50 μ l lysing buffer supplemented with protease inhibitors. A total of 10 μ l of protein per lane was separated by SDS-PAGE (8% for NRF2; 10% for DUSP1) and transferred to PVDF membranes. Membranes were blocked in 5% skim milk for 1 hour. Membranes were incubated with anti-NRF2 antibody (dilution 1:1000; Cell Signaling Technology, USA), anti-DUSP1 (dilution 1:1000; EMD Millipore, USA), or anti- β -actin antibody (dilution 1:40000; abcam, UK). Reaction with secondary antibodies (dilution 1:6000; GE Healthcare, USA) was then carried for 1 hour at RT. Band intensity was analyzed using ChemiDoc Touch imaging System (Bio-Rad).

Chromatin immunoprecipitation (ChIP)

SKM-1 cells were cross-linked with formaldehyde, collected in PBS, and resuspended in lysis buffer. For NRF2 ChIP, lysates were incubated with Micrococcal Nuclease digestion buffer (New England Biolabs, USA) to obtain chromatin fragments of 200-1000bp. The

lysates were then diluted with ChIP dilution buffer and incubated with NRF2 antibodies (dilution 1:100; Cell signaling technology, USA) overnight. The immune complexes were collected with protein G magnetic beads, washed, and eluted. The cross-links were reversed and DNA was recovered. Relative amounts of DNA in the complex were quantified by real-time PCR. *NQO1* primers were designed according to published literatures.^[13] *DUSP1* and negative control primers were designed according to published ChIP sequence (GSE37589).^[14] Primer sequences were shown in Table S5. In ChIP q-PCR analysis, the values from NRF2 immuno-precipitated samples were normalized to which from the input DNA according to published methods. The chromatin sample, which was before the NRF2 antibody pulls down, was used as the input. *NQO1* and *DUSP1* enrichments were then normalized to the negative control (the background levels)^[15,16].

Quantitative real-time polymerase chain reaction (q-PCR)

Total RNA was extracted from cells using miRNeasy Mini Kit (QIAGEN, Germany). Each reaction contained 5 μ l SYBR Green PCR Master Mix (Thermo Fisher Scientific, USA), 0.5 μ l of each primer (10 μ M), 1 μ l cDNA template and 3 μ l ddH₂O. Q-PCR primers were

designed using Primerbank. Gene expression was normalized to the housekeeping gene. The holding, cycling and melt curve parameters used were: 95°C for 10 minutes, 40 cycles of 95°C for 15 seconds and 60°C for 1 minute with a final step at 95 °C for 15 seconds, 60 °C for 1 minute and 95 °C for 15 second. Primer sequences for q-PCR analysis are provided in Table S6.

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Supplemental List 1 Leading adge gene list (MDS-EB-1/2 VS. MDS-SLD/RS)

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	RUNNING ES
ATP8B4	ATPase, Class I, type 8B, member 4	0.512580574	0.006147837
ANGPT1	angiopoietin 1	0.50246489	0.012656895
SOCS5	suppressor of cytokine signaling 5	0.481182903	0.01827966
PTTG1IP	pituitary tumor-transforming 1 interacting protein	0.445339352	0.022918493
ATG16L2	ATG16 autophagy related 16-like 2 (<i>S. cerevisiae</i>)	0.439675629	0.028427318
ABCC1	ATP-binding cassette, sub-family C (CFTR/MRP), member	0.439315379	0.034379717
DAPK1	death-associated protein kinase 1	0.425923407	0.039004616
TNRC6B	trinucleotide repeat containing 6B	0.409621149	0.042262588
VPS8	vacuolar protein sorting 8 homolog (<i>S. cerevisiae</i>)	0.40900442	0.047654808
ALS2	amyotrophic lateral sclerosis 2 (juvenile)	0.403132617	0.05226988
TFPI	tissue factor pathway inhibitor (lipoprotein-associated coag)	0.40266791	0.0576759
SSPN	sarcospan (Kras oncogene-associated gene)	0.399559796	0.0628405
CHST11	carbohydrate (chondroitin 4) sulfotransferase 11	0.395492882	0.067651026
EIF4E3	eukaryotic translation initiation factor 4E member 3	0.389652818	0.0719838
MAMDC2	MAM domain containing 2	0.387597322	0.07653786
ZBTB20	zinc finger and BTB domain containing 20	0.380793899	0.08030215
IRF2BP2	interferon regulatory factor 2 binding protein 2	0.376815975	0.084460996
SDCCAG8	serologically defined colon cancer antigen 8	0.37137863	0.08864582
YPEL5	yippee-like 5 (<i>Drosophila</i>)	0.368114412	0.093085386
CPNE8	copine VIII	0.354384124	0.094249584
WASF1	WAS protein family, member 1	0.350103736	0.09809632
CTSO	cathepsin O	0.349604964	0.10258407
FOXP1	forkhead box P1	0.34828192	0.1069044
FNBP1	formin binding protein 1	0.344996512	0.1104328
OXR1	oxidation resistance 1	0.343469828	0.11453846
CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like	0.339881659	0.11809721
RASGRP3	RAS guanyl releasing protein 3 (calcium and DAG-regulate	0.337612242	0.121974014
ARRDC4	arrestin domain containing 4	0.328931987	0.123740084
PDGFC	platelet derived growth factor C	0.328764439	0.12814477
STYK1	serine/threonine/tyrosine kinase 1	0.32801798	0.13219054
TNFRSF1A	tumor necrosis factor receptor superfamily, member 1A	0.325947791	0.13570999
COMMD6	COMM domain containing 6	0.324795485	0.13981175
DENND4C	DENN/MADD domain containing 4C	0.3201015	0.1420063
PRR13	proline rich 13	0.312308073	0.14329797
ANKRD44	ankyrin repeat domain 44	0.311325729	0.14726706
CD164	CD164 molecule, sialomucin	0.309720814	0.15106493
KLF6	Kruppel-like factor 6	0.30437687	0.15299657
MACF1	microtubule-actin crosslinking factor 1	0.302978963	0.15640412
RANBP6	RAN binding protein 6	0.301921517	0.16004647
PPP1R12A	protein phosphatase 1, regulatory (inhibitor) subunit 12A	0.290262371	0.15834874
CLASP1	cytoplasmic linker associated protein 1	0.289374799	0.16197059
ANXA1	annexin A1	0.288545072	0.16553137
LRRK1	leucine-rich repeat kinase 1	0.286271095	0.16826408
GPC6	glypican 6	0.285317868	0.17153199
LPP	LIM domain containing preferred translocation partner in li	0.282165974	0.17361115
SYNE1	spectrin repeat containing, nuclear envelope 1	0.282074958	0.17728357
PELI2	pellino homolog 2 (<i>Drosophila</i>)	0.27738747	0.1784509
ARHGDI1B	Rho GDP dissociation inhibitor (GDI) beta	0.277000219	0.18185525
ITPR2	inositol 1,4,5-triphosphate receptor, type 2	0.275294065	0.18458872
ANK3	ankyrin 3, node of Ranvier (ankyrin G)	0.27225849	0.18658346
PTPRM	protein tyrosine phosphatase, receptor type, M	0.272256583	0.19027235
ZC3H11A	zinc finger CCCH-type containing 11A	0.27200079	0.19380826
GALK2	galactokinase 2	0.269003808	0.19541012
CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	0.26837647	0.19854814
ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	0.26292178	0.19847308
PKD1	polycystic kidney disease 1 (autosomal dominant)	0.2599428	0.20015147
REV3L	REV3-like, catalytic subunit of DNA polymerase zeta (yeas	0.259468436	0.20336811
PHF3	PHD finger protein 3	0.258403212	0.20632116
JAG1	jagged 1 (Alagille syndrome)	0.256460756	0.20845066
NAPB	N-ethylmaleimide-sensitive factor attachment protein, beta	0.255532086	0.21136482

PJA2	praja 2, RING-H2 motif containing	0.254612207	0.21431635
NEK7	NIMA (never in mitosis gene a)-related kinase 7	0.25248611	0.21614285
CLN5	ceroid-lipofuscinosis, neuronal 5	0.25164327	0.21910398
GOLPH3	golgi phosphoprotein 3 (coat-protein)	0.250007272	0.22129552
LRP12	low density lipoprotein-related protein 12	0.249566227	0.22427833
CTNND1	catenin (cadherin-associated protein), delta 1	0.24955596	0.22765963
BTC	betacellulin	0.247412503	0.229816
NR1D2	nuclear receptor subfamily 1, group D, member 2	0.245555028	0.23199706
KLF12	Kruppel-like factor 12	0.244267434	0.23485824
ALDH8A1	aldehyde dehydrogenase 8 family, member A1	0.242467463	0.236549
CDADC1	cytidine and dCMP deaminase domain containing 1	0.24174796	0.23907708
DUSP1	dual specificity phosphatase 1	0.241163015	0.24189621
DPYD	dihydropyrimidine dehydrogenase	0.240695566	0.24480866
MDFIC	MyoD family inhibitor domain containing	0.23942171	0.24700625
APOL6	apolipoprotein L, 6	0.238712087	0.24964269
LAPTM4B	lysosomal associated protein transmembrane 4 beta	0.238484234	0.2527245
ZDHC17	zinc finger, DHHC-type containing 17	0.237292245	0.2549929
CEP170	centrosomal protein 170kDa	0.237021893	0.25815454
TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)	0.235627383	0.26030073
CHSY1	carbohydrate (chondroitin) synthase 1	0.234876618	0.26283535
ZYX	zyxin	0.234508827	0.2658633
MRC2	mannose receptor, C type 2	0.231846347	0.2669617
CPT1A	carnitine palmitoyltransferase 1A (liver)	0.2309241	0.26904416
GVIN1	GTPase, very large interferon inducible 1	0.228864685	0.27045095
TMEM55A	transmembrane protein 55A	0.227768883	0.27283946
MEIS1	Meis1, myeloid ecotropic viral integration site 1 homolog (t	0.222604647	0.27191916
CAPN7	calpain 7	0.221017003	0.27307013
TSPAN2	tetraspanin 2	0.217558637	0.27282888
WDSUB1	WD repeat, sterile alpha motif and U-box domain containin	0.215151355	0.27345195
SETBP1	SET binding protein 1	0.21363467	0.27525032
LAYN	layilin	0.213532329	0.2780937
L3MBTL3	l(3)mbt-like 3 (Drosophila)	0.211317107	0.27856514
GPC5	glypican 5	0.211137503	0.28132623
TMEM49	transmembrane protein 49	0.210248366	0.28347734
MAP4K3	mitogen-activated protein kinase kinase kinase kinase 3	0.208589926	0.28500804
ZZEF1	zinc finger, ZZ-type with EF-hand domain 1	0.208352357	0.28768158
PRKG1	protein kinase, cGMP-dependent, type I	0.204872832	0.2873183
ASB3	ankyrin repeat and SOCS box-containing 3	0.204075381	0.28933594
CEP290	centrosomal protein 290kDa	0.203386426	0.29149374
PBX4	pre-B-cell leukemia transcription factor 4	0.202045217	0.29323474
RTP4	receptor transporter protein 4	0.20133239	0.29521522
GSTM2	glutathione S-transferase M2 (muscle)	0.199214563	0.29577184
LNX1	ligand of numb-protein X 1	0.191016972	0.2905868
BMPR1A	bone morphogenetic protein receptor, type IA	0.190674052	0.29282147
TMEM63A	transmembrane protein 63A	0.188150391	0.29297903
PGAP1	-	0.185286909	0.292749
YAF2	YY1 associated factor 2	0.184744433	0.29505283
RNF139	ring finger protein 139	0.18436259	0.29735148
GSTM1	glutathione S-transferase M1	0.180143788	0.2960552
HACE1	HECT domain and ankyrin repeat containing, E3 ubiquitin 1	0.178745016	0.2971317
KRAS	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	0.178441465	0.29920065
PQLC3	PQ loop repeat containing 3	0.178045005	0.3013639
NETO2	neuropilin (NRP) and tolloid (TLL)-like 2	0.176678255	0.30251205
TSC2	tuberous sclerosis 2	0.174375713	0.30288157
FZD7	frizzled homolog 7 (Drosophila)	0.169527635	0.29914936
AKAP7	A kinase (PRKA) anchor protein 7	0.168995008	0.30099067
CD302	CD302 molecule	0.168476194	0.30287477
TMTC2	transmembrane and tetratricopeptide repeat containing 2	0.16796422	0.3047021
SQRDL	sulfide quinone reductase-like (yeast)	0.167653978	0.30687404
PRKAA1	protein kinase, AMP-activated, alpha 1 catalytic subunit	0.167505324	0.3089941
WAPAL	wings apart-like homolog (Drosophila)	0.165595815	0.30979282
LYPLAL1	lysophospholipase-like 1	0.163935706	0.3109178
AHR	aryl hydrocarbon receptor	0.163757518	0.31303692

CGRRF1	cell growth regulator with ring finger domain 1	0.162412837	0.31409147
TSPAN3	tetraspanin 3	0.159739003	0.31341562
MAN2A1	mannosidase, alpha, class 2A, member 1	0.157621026	0.3133588
LEMD3	LEM domain containing 3	0.157084331	0.31493908
MKL1	megakaryoblastic leukemia (translocation) 1	0.155915454	0.31625438
FAM43A	family with sequence similarity 43, member A	0.154874936	0.31695762
CCDC104	coiled-coil domain containing 104	0.153804764	0.3179952
GABARAPL1	GABA(A) receptor-associated protein like 1	0.153802201	0.3200791
ENAH	enabled homolog (Drosophila)	0.153191417	0.32170627

Supplemental List 2 Leading adge gene list (MDS VS. HC)

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	RUNNING ES
ATP8B4	ATPase, Class I, type 8B, member 4	0.512580574	0.006147837
ANGPT1	angiopoietin 1	0.50246489	0.012656895
SOCS5	suppressor of cytokine signaling 5	0.481182903	0.01827966
PTTG1IP	pituitary tumor-transforming 1 interacting protein	0.445339352	0.022918493
ATG16L2	ATG16 autophagy related 16-like 2 (<i>S. cerevisiae</i>)	0.439675629	0.028427318
ABCC1	ATP-binding cassette, sub-family C (CFTR/MRP), mem	0.439315379	0.034379717
DAPK1	death-associated protein kinase 1	0.425923407	0.039004616
TNRC6B	trinucleotide repeat containing 6B	0.409621149	0.042262588
VPS8	vacuolar protein sorting 8 homolog (<i>S. cerevisiae</i>)	0.40900442	0.047654808
ALS2	amyotrophic lateral sclerosis 2 (juvenile)	0.403132617	0.05226988
TFPI	tissue factor pathway inhibitor (lipoprotein-associated c	0.40266791	0.0576759
SSPN	sarcospan (Kras oncogene-associated gene)	0.399559796	0.0628405
CHST11	carbohydrate (chondroitin 4) sulfotransferase 11	0.395492882	0.067651026
EIF4E3	eukaryotic translation initiation factor 4E member 3	0.389652818	0.0719838
MAMDC2	MAM domain containing 2	0.387597322	0.07653786
ZBTB20	zinc finger and BTB domain containing 20	0.380793899	0.08030215
IRF2BP2	interferon regulatory factor 2 binding protein 2	0.376815975	0.084460996
SDCCAG8	serologically defined colon cancer antigen 8	0.37137863	0.08864582
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CPNE8	copine VIII	0.354384124	0.094249584
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CTSO	cathepsin O	0.349604964	0.10258407
FOXP1	forkhead box P1	0.34828192	0.1069044
FNBP1	formin binding protein 1	0.344996512	0.1104328
OXR1	oxidation resistance 1	0.343469828	0.11453846
CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-	0.339881659	0.11809721
RASGRP3	RAS guanyl releasing protein 3 (calcium and DAG-regu	0.337612242	0.121974014
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DENND4C	DENN/MADD domain containing 4C	0.3201015	0.1420063
PRR13	proline rich 13	0.312308073	0.14329797
ANKRD44	ankyrin repeat domain 44	0.311325729	0.14726706
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KLF6	Kruppel-like factor 6	0.30437687	0.15299657
MACF1	microtubule-actin crosslinking factor 1	0.302978963	0.15640412
RANBP6	RAN binding protein 6	0.301921517	0.16004647
PPP1R12A	protein phosphatase 1, regulatory (inhibitor) subunit 12/	0.290262371	0.15834874
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ANXA1	annexin A1	0.288545072	0.16553137
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GPC6	glypican 6	0.285317868	0.17153199
LPP	LIM domain containing preferred translocation partner i	0.282165974	0.17361115
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PELI2	pellino homolog 2 (<i>Drosophila</i>)	0.27738747	0.1784509
ARHGDI1	Rho GDP dissociation inhibitor (GDI) beta	0.277000219	0.18185525
ITPR2	inositol 1,4,5-triphosphate receptor, type 2	0.275294065	0.18458872
ANK3	ankyrin 3, node of Ranvier (ankyrin G)	0.27225849	0.18658346
PTPRM	protein tyrosine phosphatase, receptor type, M	0.272256583	0.19027235
ZC3H11A	zinc finger CCCH-type containing 11A	0.27200079	0.19380826
GALK2	galactokinase 2	0.269003808	0.19541012
CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	0.26837647	0.19854814
ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	0.26292178	0.19847308
PKD1	polycystic kidney disease 1 (autosomal dominant)	0.2599428	0.20015147
REV3L	REV3-like, catalytic subunit of DNA polymerase zeta (γ)	0.259468436	0.20336811
PHF3	PHD finger protein 3	0.258403212	0.20632116
JAG1	jagged 1 (Alagille syndrome)	0.256460756	0.20845066
NAPB	N-ethylmaleimide-sensitive factor attachment protein, b	0.255532086	0.21136482

PJA2	praja 2, RING-H2 motif containing	0.254612207	0.21431635
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LRP12	low density lipoprotein-related protein 12	0.249566227	0.22427833
CTNND1	catenin (cadherin-associated protein), delta 1	0.24955596	0.22765963
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NR1D2	nuclear receptor subfamily 1, group D, member 2	0.245555028	0.23199706
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ALDH8A1	aldehyde dehydrogenase 8 family, member A1	0.242467463	0.236549
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DUSP1	dual specificity phosphatase 1	0.241163015	0.24189621
DPYD	dihydropyrimidine dehydrogenase	0.240695566	0.24480866
MDFIC	MyoD family inhibitor domain containing	0.23942171	0.24700625
APOL6	apolipoprotein L, 6	0.238712087	0.24964269
LAPTM4B	lysosomal associated protein transmembrane 4 beta	0.238484234	0.2527245
ZDHHC17	zinc finger, DHHC-type containing 17	0.237292245	0.2549929
CEP170	centrosomal protein 170kDa	0.237021893	0.25815454
TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)	0.235627383	0.26030073
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ZYX	zyxin	0.234508827	0.2658633
MRC2	mannose receptor, C type 2	0.231846347	0.2669617
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GVIN1	GTPase, very large interferon inducible 1	0.228864685	0.27045095
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L3MBTL3	l(3)mbt-like 3 (Drosophila)	0.211317107	0.27856514
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RTP4	receptor transporter protein 4	0.20133239	0.29521522
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LNX1	ligand of numb-protein X 1	0.191016972	0.2905868
BMPRI1A	bone morphogenetic protein receptor, type IA	0.190674052	0.29282147
TMEM63A	transmembrane protein 63A	0.188150391	0.29297903
PGAP1	-	0.185286909	0.292749
YAF2	YY1 associated factor 2	0.184744433	0.29505283
RNF139	ring finger protein 139	0.18436259	0.29735148
GSTM1	glutathione S-transferase M1	0.180143788	0.2960552
HACE1	HECT domain and ankyrin repeat containing, E3 ubiquitin	0.178745016	0.2971317
KRAS	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	0.178441465	0.29920065
PQLC3	PQ loop repeat containing 3	0.178045005	0.3013639
NETO2	neuropilin (NRP) and tolloid (TLL)-like 2	0.176678255	0.30251205
TSC2	tuberous sclerosis 2	0.174375713	0.30288157
FZD7	frizzled homolog 7 (Drosophila)	0.169527635	0.29914936
AKAP7	A kinase (PRKA) anchor protein 7	0.168995008	0.30099067
CD302	CD302 molecule	0.168476194	0.30287477
TMTC2	transmembrane and tetratricopeptide repeat containing 2	0.16796422	0.3047021
SQRDL	sulfide quinone reductase-like (yeast)	0.167653978	0.30687404
PRKAA1	protein kinase, AMP-activated, alpha 1 catalytic subunit	0.167505324	0.3089941
WAPAL	wings apart-like homolog (Drosophila)	0.165595815	0.30979282
LYPLAL1	lysophospholipase-like 1	0.163935706	0.3109178
AHR	aryl hydrocarbon receptor	0.163757518	0.31303692

CGRRF1	cell growth regulator with ring finger domain 1	0.162412837	0.31409147
TSPAN3	tetraspanin 3	0.159739003	0.31341562
MAN2A1	mannosidase, alpha, class 2A, member 1	0.157621026	0.3133588
LEMD3	LEM domain containing 3	0.157084331	0.31493908
MKL1	megakaryoblastic leukemia (translocation) 1	0.155915454	0.31625438
FAM43A	family with sequence similarity 43, member A	0.154874936	0.31695762
CCDC104	coiled-coil domain containing 104	0.153804764	0.3179952
GABARAPL1	GABA(A) receptor-associated protein like 1	0.153802201	0.3200791
ENAH	enabled homolog (Drosophila)	0.153191417	0.32170627

Supplemental List 3 Leading adge gene list (Ara-C resistant VS. sensitive AML)

PROBE	RANK METRIC SCORE	RUNNING ES	RE ENRICHMENT
BCL6	3.087686777	0.01179857	Yes
ABHD5	2.603085041	0.021068387	Yes
KLF4	2.239661217	0.028474566	Yes
GABARAPL1	2.053781509	0.03499846	Yes
QPCT	1.941035271	0.041414943	Yes
FGL2	1.855325103	0.04769719	Yes
PTX3	1.831896186	0.05454532	Yes
RAB10	1.831192255	0.06162047	Yes
SCPEP1	1.828486919	0.06865235	Yes
MEGF9	1.797686458	0.07526984	Yes
TPM1	1.783013344	0.08186346	Yes
SNX13	1.728109717	0.08749009	Yes
KREMEN1	1.72793746	0.094166294	Yes
TMEM55A	1.55259347	0.096948646	Yes
OSCAR	1.510194302	0.10160203	Yes
MAN2A1	1.42419076	0.10418366	Yes
VCAN	1.389169216	0.10800842	Yes
AOX1	1.372419596	0.11301564	Yes
GRK5	1.370033622	0.118276194	Yes
PPARD	1.34531188	0.122358166	Yes
SGOL2	1.292798877	0.124924436	Yes
MAML2	1.262726903	0.12832631	Yes
C1GALT1	1.232173681	0.13131474	Yes
CTNNA1	1.215638399	0.13525672	Yes
SRXN1	1.211660147	0.13964282	Yes
CBARA1	1.207622766	0.14421023	Yes
PRKCD	1.173778534	0.14703868	Yes
CD302	1.172761679	0.15140577	Yes
CD9	1.168833017	0.15565921	Yes
HMOX1	1.168082833	0.1601395	Yes
EPHB3	1.156487823	0.1639514	Yes
MARCKS	1.14480114	0.16768533	Yes
SNX22	1.113311768	0.17054272	Yes
AIM1	1.097683907	0.17353666	Yes
MCFD2	1.095256567	0.17760429	Yes
VPS8	1.076269269	0.18035138	Yes
LILRB4	1.073344231	0.18417025	Yes
FMNL2	1.069604516	0.1880403	Yes
SNX1	1.052069187	0.19069389	Yes
JAG1	1.047079086	0.19424717	Yes
TANC2	1.034207463	0.19712713	Yes
SERPINB9	1.029946804	0.20074551	Yes
SLC1A4	1.017757773	0.20339781	Yes
CDC42EP3	1.011045933	0.20684469	Yes
CXCL5	1.004606247	0.21013542	Yes
RXRA	1.004367113	0.21401596	Yes
PKM2	0.997572839	0.21727951	Yes
CTSB	0.994615436	0.22085983	Yes
ZYX	0.990587652	0.22442459	Yes
EIF4E3	0.978834569	0.22712342	Yes
ENC1	0.974402428	0.23036309	Yes
CEBPB	0.963928342	0.23270896	Yes
FYN	0.957736611	0.23594986	Yes
BTG1	0.953296423	0.23937054	Yes
PLA2G4A	0.932439625	0.24077424	Yes
TCF7L2	0.92872566	0.24406716	Yes
LACTB	0.916652024	0.24646011	Yes
OAT	0.89931643	0.24809685	Yes
TTC35	0.890878379	0.25055432	Yes
DPYD	0.871483803	0.2515584	Yes

PRKAR2B	0.848592997	0.2520474	Yes
RANBP6	0.845996201	0.2550535	Yes
KCNJ2	0.836691737	0.2574657	Yes
CDKN2B	0.828617096	0.25964978	Yes
RGMA	0.822977006	0.26227155	Yes
TGM3	0.815649331	0.26443836	Yes
P4HA1	0.799351037	0.26499963	Yes
TRIB1	0.795005262	0.26767746	Yes
CYP1B1	0.792108953	0.27027842	Yes
CAPN7	0.787232876	0.27279493	Yes
SYNE1	0.786062062	0.27576637	Yes
NPEPPS	0.775351644	0.27712107	Yes
HIPK2	0.76516068	0.2785677	Yes
RAB24	0.764496326	0.2813902	Yes
MRV11	0.760595441	0.2837381	Yes
LPP	0.75542891	0.28580353	Yes
INSIG2	0.755341887	0.28872195	Yes
EPHX1	0.753674924	0.29124007	Yes
TUBE1	0.751011074	0.2937807	Yes
ATP8B4	0.750623167	0.29661524	Yes
PRR13	0.745013773	0.29883733	Yes
PTGS2	0.741352201	0.30111092	Yes
ANKRD44	0.738396764	0.3033731	Yes
DAP	0.729586303	0.3049448	Yes
OXR1	0.722235858	0.30678353	Yes
FBXL3	0.722156048	0.3095737	Yes
LAPTM4B	0.715071559	0.3111878	Yes
MMD	0.706893802	0.3122278	Yes
ST3GAL2	0.695070446	0.31299433	Yes
IQWD1	0.692535043	0.31514493	Yes
PELI2	0.691564977	0.31771848	Yes
TMEM63A	0.689603031	0.32015315	Yes
LPL	0.682872295	0.32131463	Yes
AKAP7	0.680244386	0.3233193	Yes
RGS10	0.673204184	0.32477164	Yes
TNFRSF1A	0.671906352	0.32723638	Yes
RGNEF	0.669132233	0.32926378	Yes
CPNE8	0.663057387	0.3305128	Yes
KIF26B	0.648847461	0.32993463	Yes
CCDC109B	0.643876135	0.33124083	Yes
NETO2	0.625436544	0.32909533	Yes
CLN5	0.620747566	0.33044344	Yes
CDC42BPA	0.600748062	0.32793996	Yes
FSHR	0.595677793	0.3289615	Yes
SPRED1	0.595024049	0.33106357	Yes
ADAM23	0.591364801	0.332692	Yes
CDKN1A	0.586151302	0.33374235	Yes
MYH9	0.582894742	0.3350755	Yes
IFIT3	0.580168664	0.33646378	Yes
DAAM2	0.578890085	0.3384707	Yes
DUSP1	0.577115893	0.34017536	Yes
TBC1D23	0.553900599	0.33548883	Yes
E2F6	0.551728189	0.33696413	Yes
BMP8A	0.54860121	0.33809915	Yes
RAF1	0.548181832	0.3401187	Yes
GAS1	0.511906624	0.3311346	Yes
GSTA4	0.509432793	0.33228236	Yes
RAI14	0.507881165	0.33375236	Yes
KLF6	0.497347772	0.33199808	Yes
NAV1	0.495159268	0.33305788	Yes
UNC5B	0.485675126	0.33142263	Yes
EEA1	0.485522568	0.33326572	Yes
BLVRB	0.483899534	0.33438048	Yes

CORO7	0.476564914	0.33339924	Yes
SIPA1L2	0.475778401	0.3349093	Yes
NSMCE2	0.474522352	0.33621758	Yes
TRAM2	0.468325406	0.33592653	Yes
IDH1	0.462249994	0.33564484	Yes
MKL1	0.452658117	0.333882	Yes
PLXDC2	0.452482879	0.3355646	Yes
MAP3K9	0.452277511	0.33721364	Yes
HFE	0.451663673	0.33872896	Yes
MEIS1	0.451530814	0.34044072	Yes
TMTC2	0.451257885	0.34205297	Yes
F3	0.451071918	0.34373012	Yes
HINT3	0.449773043	0.3451397	Yes
PTPRK	0.446438581	0.3455518	Yes
MLYCD	0.445966154	0.34704512	Yes
SOCS3	0.440079391	0.3462511	Yes
CLCN1	0.434311509	0.34576303	Yes
FKBPL	0.434163094	0.34740767	Yes
SQRDL	0.433314264	0.34872082	Yes
FTH1	0.426686704	0.34800637	Yes
PJA2	0.422096878	0.347668	Yes
KLHDC8A	0.420109719	0.3485363	Yes
GZF1	0.419532895	0.34989467	Yes
ZC3H11A	0.418028384	0.35091904	Yes
RSPO2	0.416052282	0.35147628	Yes
SPP2	0.41532442	0.35291687	Yes
LEMD3	0.411956728	0.35303164	Yes
FAM69A	0.410624683	0.35415867	Yes
YIPF5	0.40675965	0.35412207	Yes
PQLC3	0.40583539	0.35516497	Yes