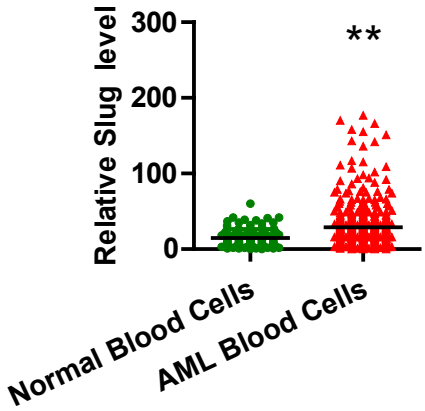
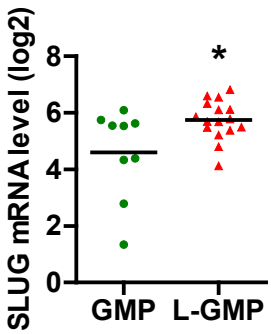
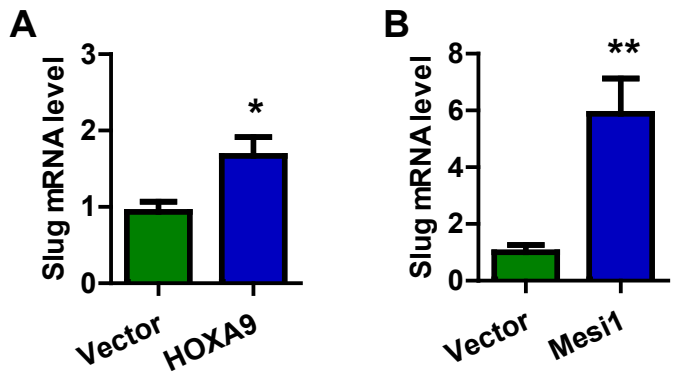


Supplemental Figure 1. The expression of SLUG between normal hematopoietic cells of healthy controls and AML blasts and mononuclear cells of patients. The data were obtained from a public microarray database Gene Expression Omnibus (GSE1159, GSE7638, GSE3365, GSE12417, and GSE1140) (normal samples n = 107, AML samples n = 456). All data are represented as mean ± SD. Two-tailed Student's *t*-tests were used to assess statistical significance (** $P < 0.01$).

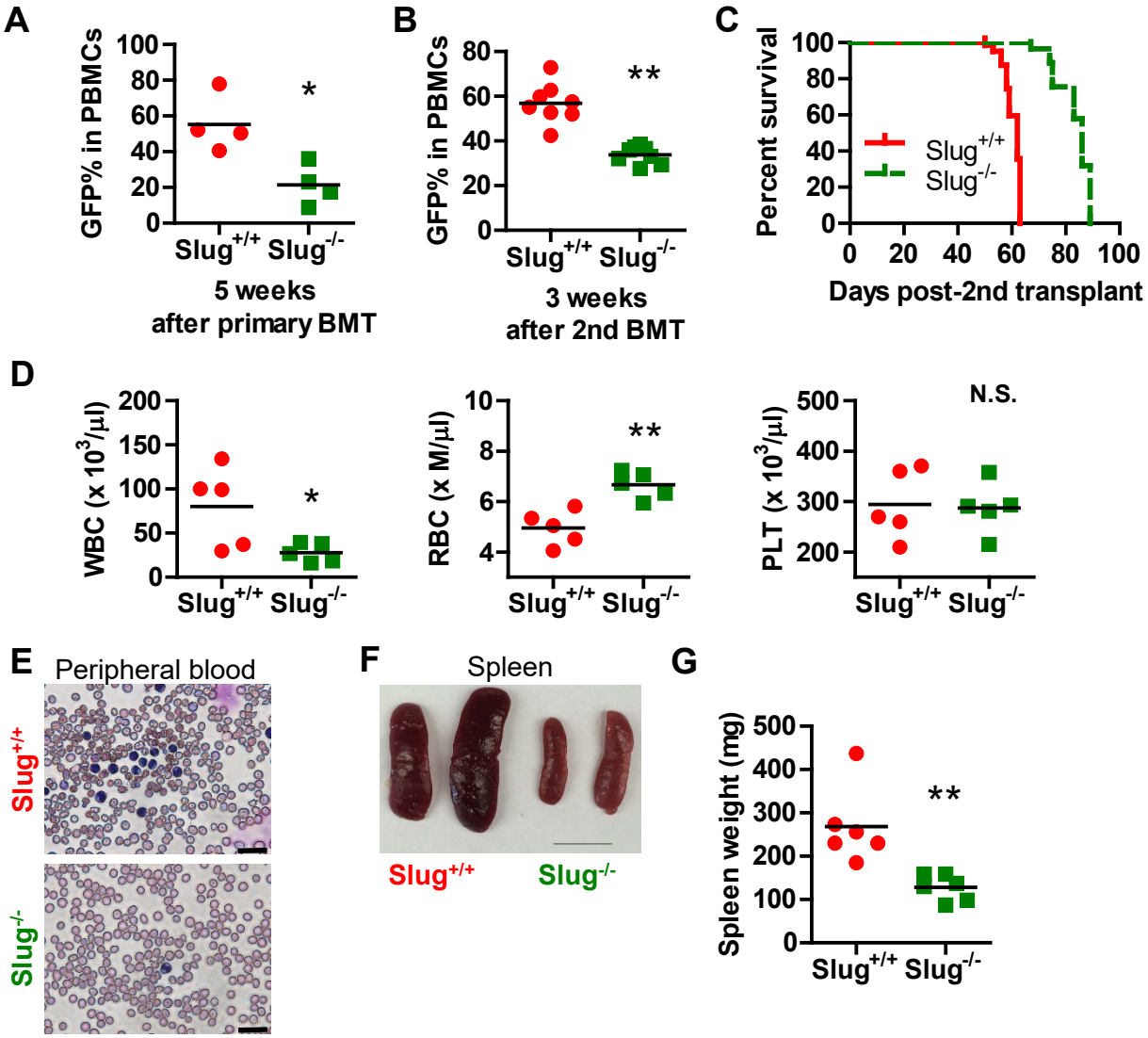


Supplemental Figure 2. The expression of SLUG between normal GMPs and AML patients' L-GMPs (normal patient, n = 9; AML patient n = 16). All data are represented as mean ± SD. Two-tailed Student's *t*-tests were used to assess statistical significance (* $P < 0.05$).



Supplemental Figure 3. qPCR analysis of the expression of endogenous *Slug* in mouse HSPCs transduced with retroviral vector only or retrovirus expressing HoxA9 (A), or Mesi1 (B) oncogene. Results are normalized to *Gapdh* expression and expressed relative to *Slug* expression in vector group (n = 3).

Supplemental Figure 4. Colony morphology of *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells at passage 3 (scale bar = 100 μm).



Supplemental Figure 5. Phenotype analysis in MLL-AF9 derived AML mice.

(**A**) GFP percentage in peripheral blood at week 5 after primary BMT with 1X10^3 AML cells (n = 4).

(**B**) GFP percentage in peripheral blood at week 3 after secondary transplantation (n = 8).

(**C**) Survival analysis of secondary recipient mice. Median survival was 62 versus 86 days post-transplant for secondary recipients of *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells (5X10^5 AML GFP$^+$ cells injected), respectively ($P < 0.01$, Mantel-Cox test; n = 10).

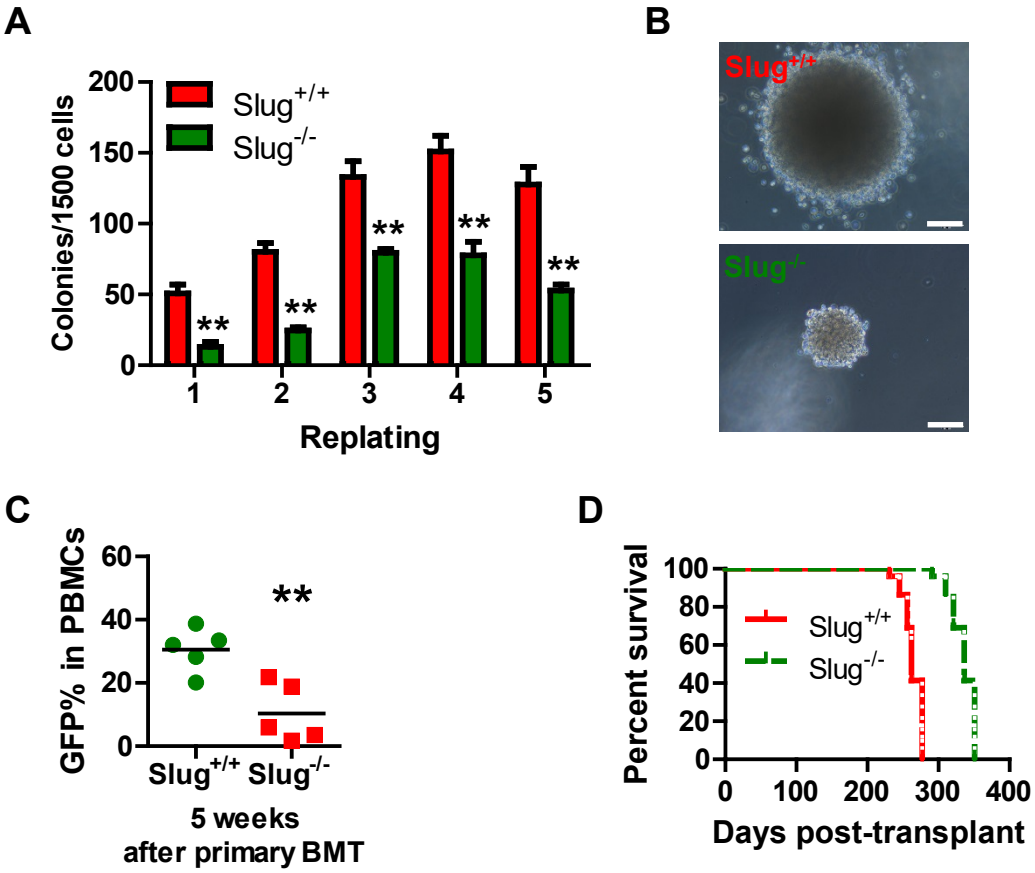
(**D**) Complete blood count (CBC) analysis of peripheral blood in the secondary recipients injected with 5X10^4 Slug$^{+/+}$ or Slug$^{-/-}$ AML cells at week 7 post-transplantation (n = 5).

(**E**) Representative peripheral blood smear stained by Wright-Giemsa (scale bar = 20 μm).

(F) Spleen morphology from the secondary recipients injected with 5X10^4 Slug$^{+/+}$ or Slug$^{-/-}$ AML cells at week 7 post-transplantation (scale bar = 1 cm).

(**G**) Spleen weight from secondary recipients of Slug$^{+/+}$ or Slug$^{-/-}$ AML cells 49 days posttransplant (n = 6).

Data are representative of two to three independent experiments. All data are represented as mean ± SD. Two-tailed Student's *t*-tests were used to assess statistical significance (*$P < 0.05$; ** $P < 0.01$; N.S, no significance).



Supplemental Figure 6. Phenotype analysis in NUP98-HoxA9 derived AML mice.

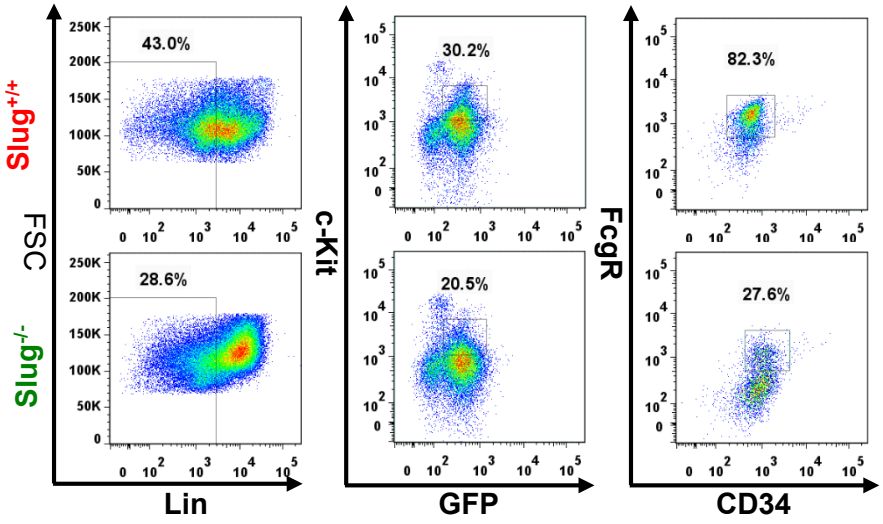
(**A**) Colony-forming assay of *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells (n = 3).

(**B**) Colony morphology of *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells at passage 3 (scale bar = 100 μm)..

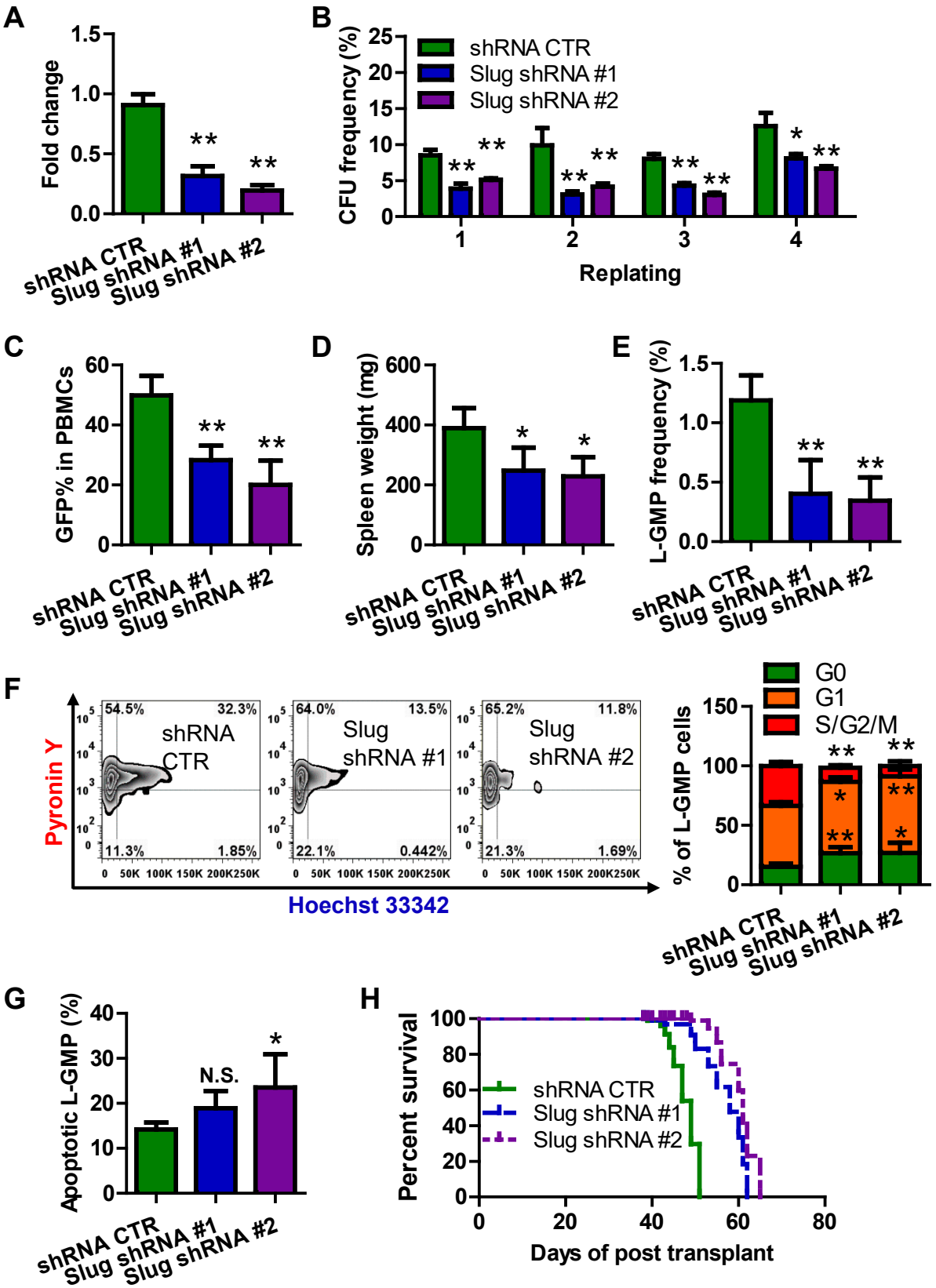
(**C**) GFP percentage in peripheral blood at week 5 after primary BMT (n = 5).

(**D**) Survival analysis of primary recipient mice. Median survival was 262 versus 336 days post-transplant for primary recipients of *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells, respectively ($P < 0.01$, Mantel-Cox test; n = 5).

Data are representative of three independent experiments. All data are represented as mean ± SD. Two-tailed Student's *t*-tests were used to assess statistical significance (*$P < 0.05$; ** $P < 0.01$; N.S, no significance).



Supplemental Figure 7. Representative flow cytometry analysis of L-GMP in the BM. BM were isolated from secondary recipients injected with 5X10^4 *Slug*$^{+/+}$ or *Slug*$^{-/-}$ AML cells at week 7 post-transplantation.



Supplemental Figure 8

Supplemental Figure 8. Knockdown of endogenous Slug suppresses self-renewal of L-GMP.

(**A**) qPCR analysis of *Slug* knockdown in L-GMP cells (n = 3).

(**B**) Colony-forming assay of AML cells by knockdown of endogenous *Slug* (n = 3).

(**C**) GFP percentage in peripheral blood at week 3 after transplantation with $1X10^5$ AML cells (n = 9).

(**D**) Spleen weight from the recipients of at week 3 post-transplantation (n= 4).

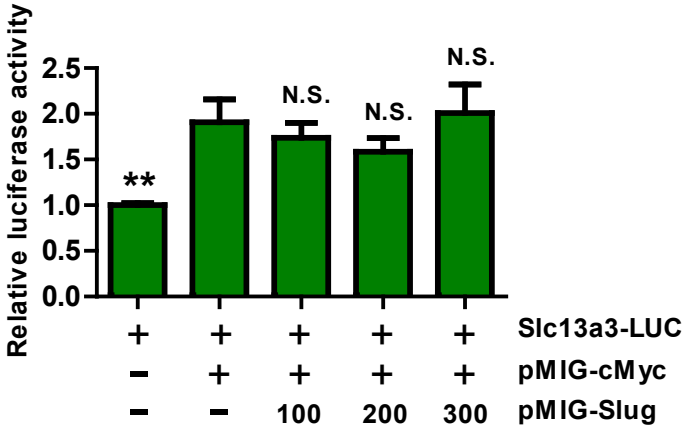
(E) Percentage of apoptotic L-GMP cells in the BM from recipients injected with AML cells at week 3 post-transplantation (n= 4).

(**F**) Quantification of L-GMP in the BM from recipients at week 3 post-transplantation (n= 4). The recipient mice were injected with $1X10^5$ AML cells infected by shRNA CTR, Slug shRNA #1, and Slug shRNA #2, respectively.

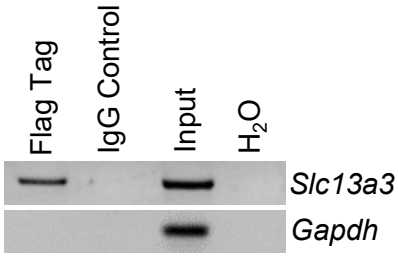
(**G**) Cell cycle phase distribution of L-GMP cells in BM from recipients injected with AML cells at week 3 post-transplantation (n= 4).

(**H**) Median survival was 49 versus 58 and 61 days post-transplant for recipients of $1X10^5$ AML cells infected by shRNA CTR, *Slug* shRNA #1 and *Slug* shRNA #2, respectively ($P < 0.01$, Mantel-Cox test; n = 10).

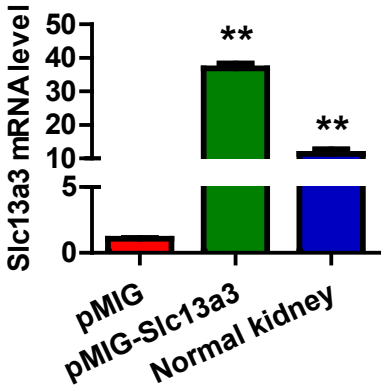
Data are representative of two to three independent experiments. All data are represented as mean ± SD. Two-tailed Student's *t*-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$; N.S, no significance).



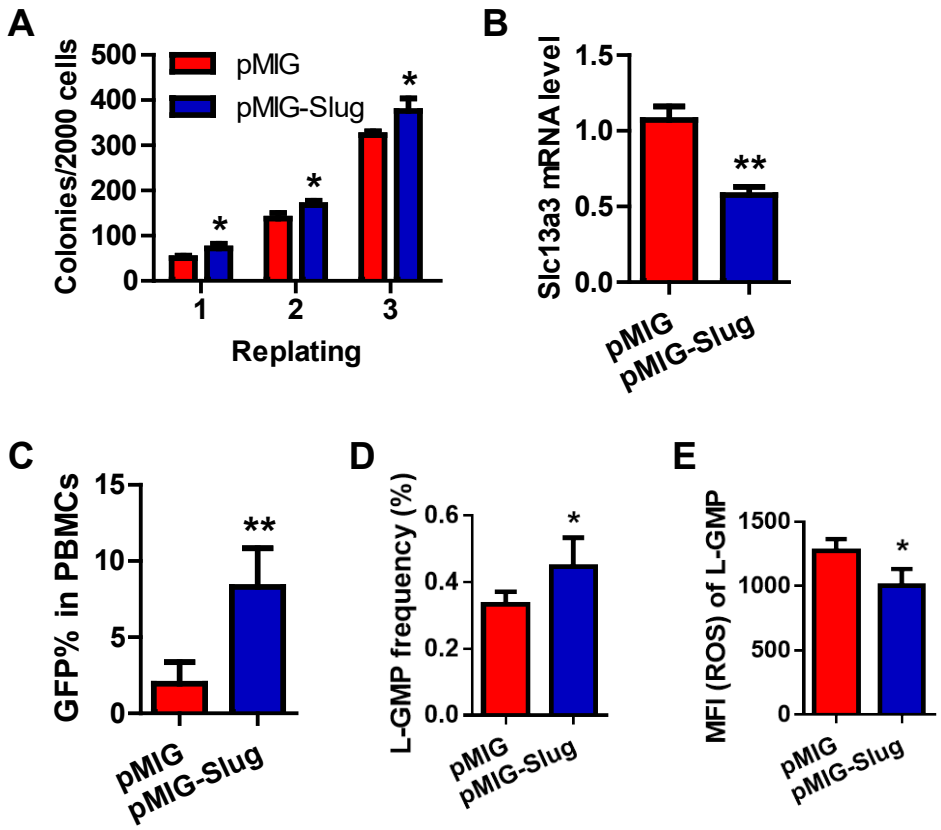
Supplemental Figure 9. Slc13a3 luciferase reporter assays. 293T cells were transfected with Slc13a3-Luc together with 400 ng of pMIG (vector control), or pMIG-cMyc with different dose of pMIG-Slug (100, 200, or 300 ng), then cultured for 72 h before luciferase activity assay. 50 ng of pCMV-LacZ was included in each transfection as an internal control to normalized luciferase activity (n = 3). Data are representative of two independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (** $P < 0.01$; N.S., not significant).



Supplemental Figure 10. Analysis of *Slug* occupancy at the Slc13a3 promoter by ChIP assay. PCR results were repeated three times.



Supplemental Figure 11. qPCR analysis of the expression of *Slc13a3* in mouse LSCs transduced with retroviral vector only or retrovirus expressing *Slc13a3* and normal mouse kidney tissue. Results are normalized to *Hprt* expression and expressed relative to *Slc13a3* expression in vector group (n = 3). Data are representative of two independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (** $P < 0.01$).



Supplemental Figure 12. Forced-expression of *Slug* enhances self-renewal of L-GMP.

(**A**) Colony-forming assay of MLL-AF9-driven AML cells by overexpression of *Slug* (n = 3).

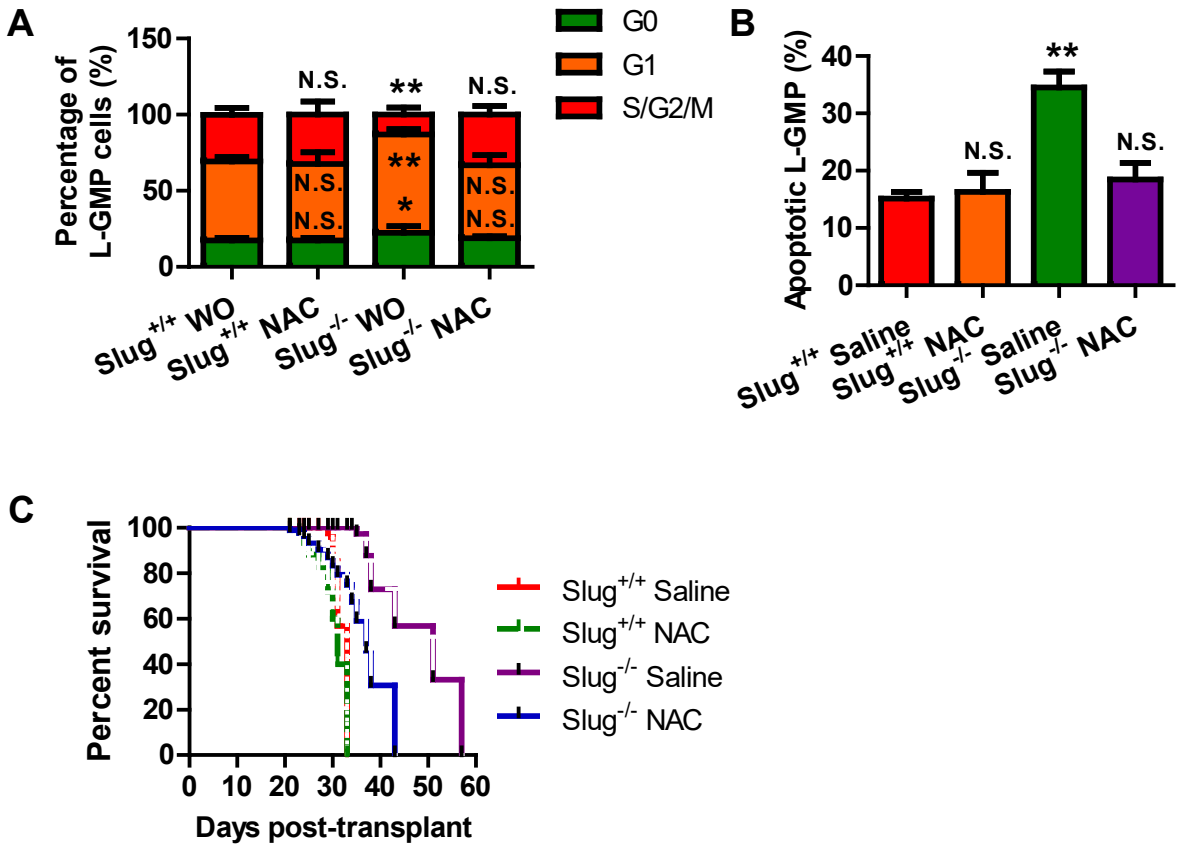
(**B**) qPCR analysis of Slc13a3 expression in MLL-AF9-driven AML cells infected with retroviral vector pMIG and pMIG-Slug, respectively (n = 3).

(**C**) GFP percentage in peripheral blood at week 2 after transplantation with $5X10^4$ AML cells infected with retroviral vector pMIG and pMIG-Slug, respectively (n = 6).

(**D**) Frequency of L-GMP in the BM from primary recipients injected with $5X10^4$ AML cells infected with retroviral vector pMIG and pMIG-Slug, respectively, at week 2 post-transplantation (n = 5).

(**E**) Flow cytometric analysis of ROS levels in L-GMPs from recipient mice injected with $5X10^4$ AML cells carrying pMIG vector and pMIG-Slug, respectively. Levels of ROS were evaluated by flow cytometry. MFI, median fluorescence intensity (n = 4)

Data are representative of two to three independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance ((* $P < 0.05$; ** $P < 0.01$).



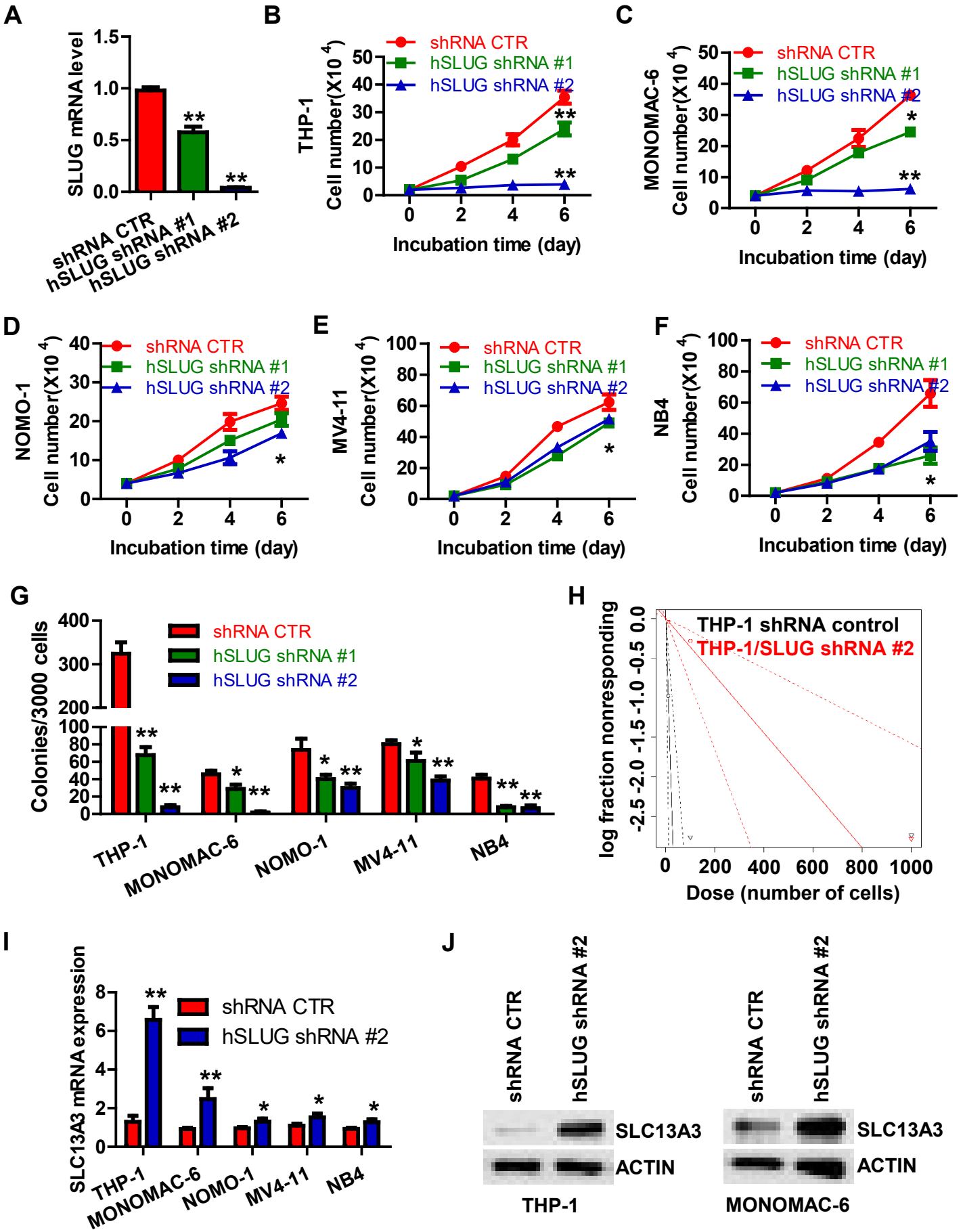
Supplemental Figure 13. Administration of NAC impairs the functions of Slug on MLL-AF9-deriven L-GMPs.

(**A**) Cell cycle phase distribution of L-GMP cells in BM from recipients injected with AML cells of *Slug*$^{+/+}$ and *Slug*$^{-/-}$ mice and then treated with saline or NAC (n= 5)

(**B**) Percentage of apoptotic L-GMP cells in the BM from recipients injected with AML cells of pMIG or pMIG-Slc13a3 and then treated with saline or NAC (n= 4).

(**C**) Survival analysis of *Slug*$^{+/+}$- or *Slug*$^{-/-}$-AML recipient mice with saline or NAC treatment. Median survival was 33, 31, 51, and 37 days post-transplant for *Slug*$^{+/+}$- or *Slug*$^{-/-}$-AML recipients treated with saline or NAC, respectively ($P < 0.05$, Mantel-Cox test; n = 6).

Data are representative of three independent experiments. Excluding survival analysis, all data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$; N.S, no significance).



Supplemental Figure 14

Supplemental Figure 14. Knockdown of SLUG impairs human AML cells.

(**A**) qPCR analysis of SLUG inducible knockdown in THP-1 cells. THP-1 cells were transduced with lenitiviruses containing inducible scramble shRNA (CTR) or hSLUG shRNAs. After puromycin selection, 1μg/ml of doxycycline were added into medium for 48 hrs.

(**B-F**) Inducible knockdown of endogenous SLUG suppresses the growths of THP-1 (B), NOMOMAC-6 (C), NOMO-1 (D), MV4-11 (E), and NB4 (F) cells (n = 3).

(**G**) Colony-forming assay of human leukemia cells by inducible knockdown of endogenous SLUG. (n = 3).

(**H**) Limiting dilution assay of THP-1 cells infected with control shRNA and SLUG shRNA #2. LSC/LICs frequencies calculated by ELDA software (n = 8).

(**I**) qPCR analysis of the expression level of *SLC13A3* in human AML cells transduced with Scramble shRNA (shRNA CTR) or hSLUG shRNA #2. Results are normalized to *HPRT* expression and expressed relative to *SLC13A3* expression in shRNA CTR group (n = 3).

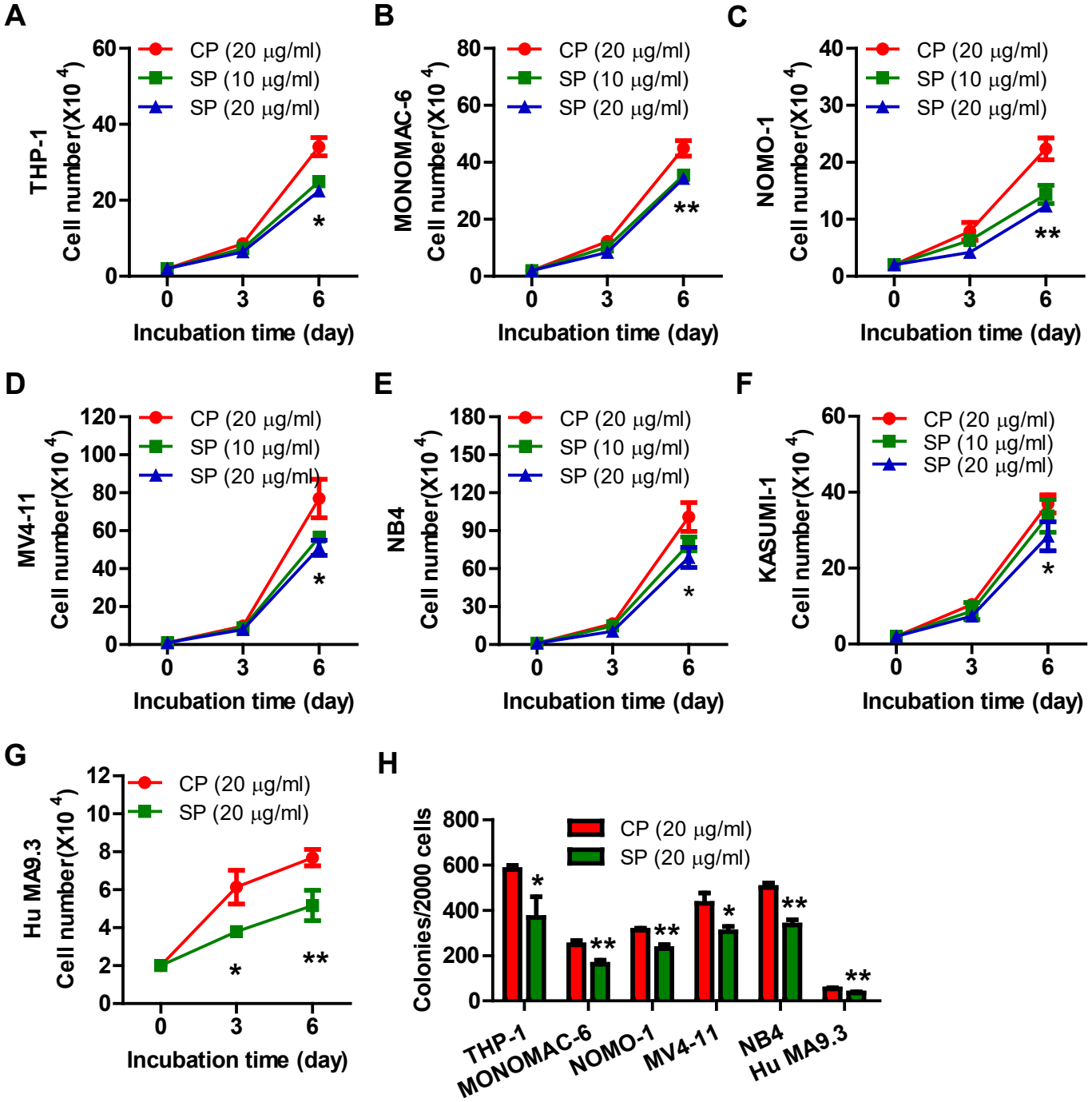
(**J**) Western blotting analysis of protein level of SLC13A3 in THP-1 and MONOMAC-6 transduced with scramble shRNA (shRNA CTR) or hSLUG shRNA #2.

Data are representative of two to three independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$).

Control peptide (TAT-GS-HA): YGRKKRRQRRRGSYPYDVPDYA

SNAG peptide (TAT-GS-HA-SNAG): YGRKKRRQRRRGSYPYDVPDYAMPRSFLVKK

Supplemental Figure 15. The peptide sequences of control peptide and SNAG peptide.

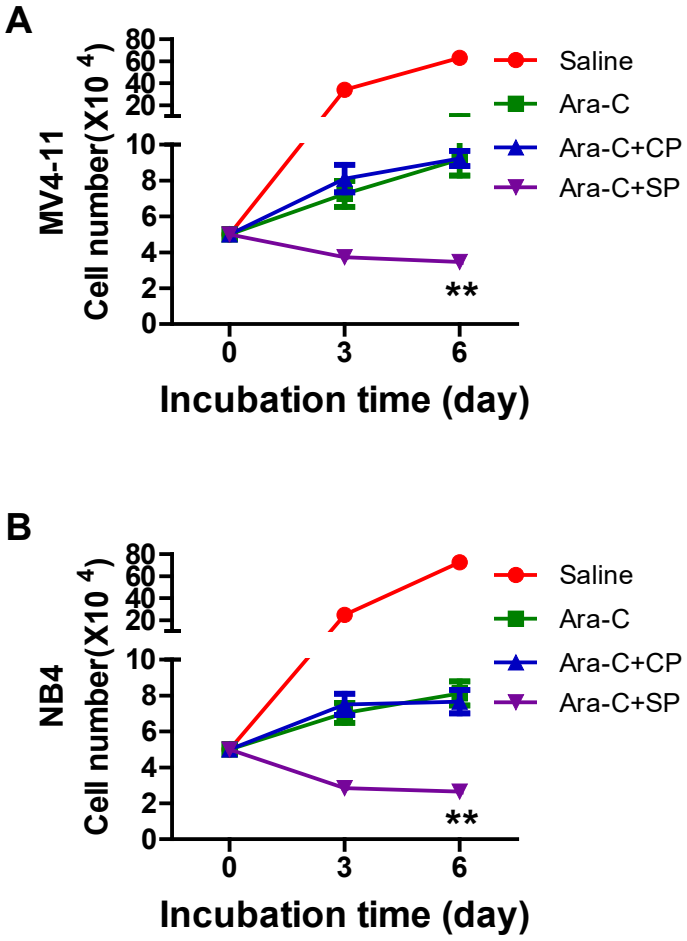


Supplemental Figure 16. Pharmacological targeting of SLUG by TAT-SNAG peptide inhibits human AML cell growth.

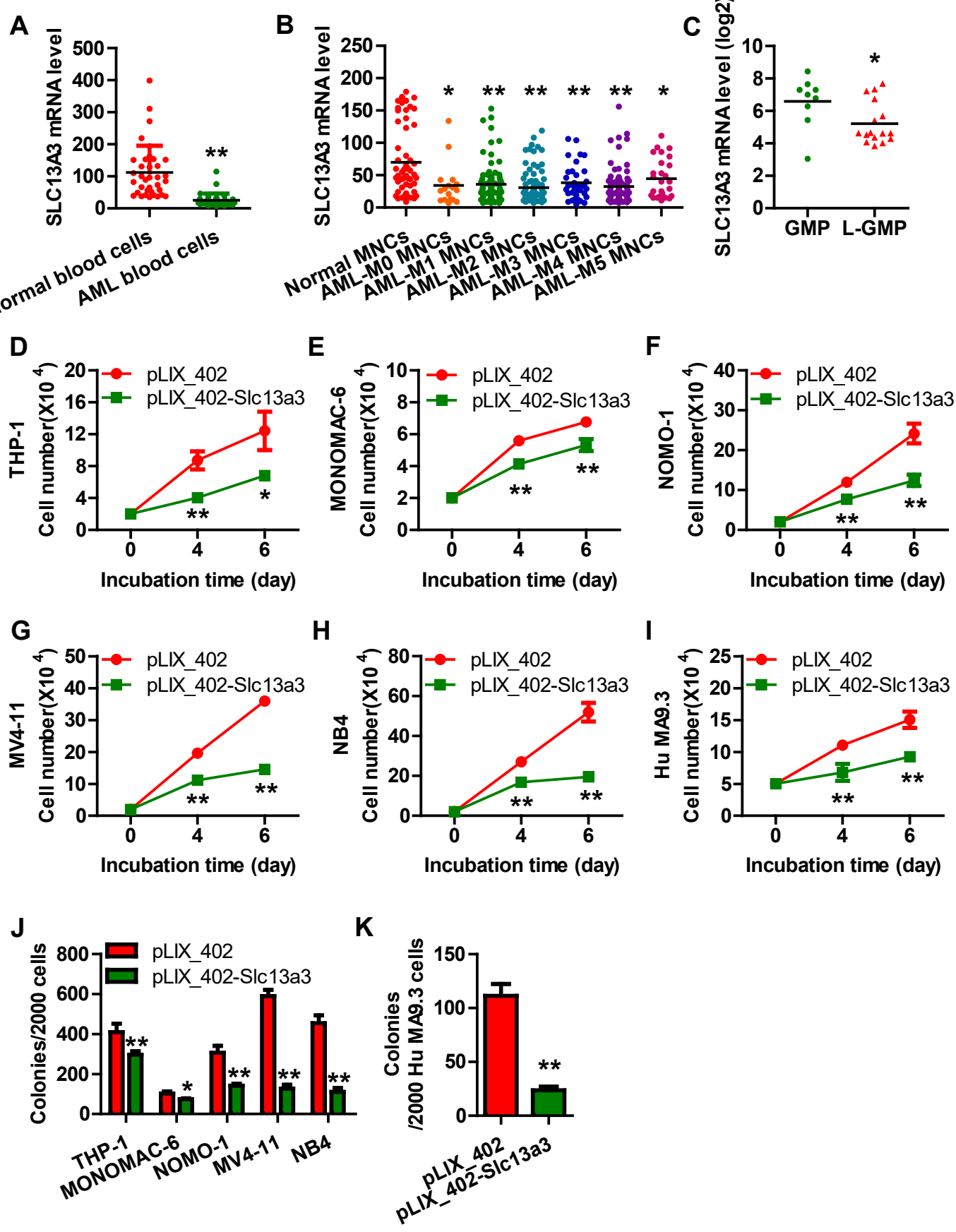
(**A-G**) The proliferation/cell growth of human AML cells. The cells were cultured in RPMI1640 or IMDM containing 10% fetal bovine serum treated with or without TAT-SNAG peptide. The cell number was counted at different time points (n = 3). (A) THP-1, (B) NOMO-1, (C) NOMOMAC-6, (**D**) NB4, (E) MV4-11, (F) KASUMI-1, and (G) Hu MA9.3.

(**H**) Colony-forming assay of human leukemic cells (n = 3).

Data are representative of two to three independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$).



Supplemental Figure 17. Enhancement of the cytotoxic effects of cytarabine in synergism with TAT-SNAG peptide in human AML cell line MV4-11 (A) and NB4 (B). The cells were cultured in RPMI1640 containing 10% fetal bovine serum treated with saline, cytarabine, combination of cytarabine and TAT-control peptide, or combination of cytarabine and TAT-SNAG peptide. The cell number was counted at different time points (n = 3). Data are representative of three independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$).



Supplemental Figure 18

Supplemental Figure 18. Forced-expression of SLC13A3 suppresses human AML cell growth.

(**A**) The expression of SLUG between normal hematopoietic cells of healthy controls and AML blasts and mononuclear cells of patients. The data were obtained from a public microarray database (GSE6613, GSE1751, and GSE8970) (normal samples n = 36, AML samples n = 34).

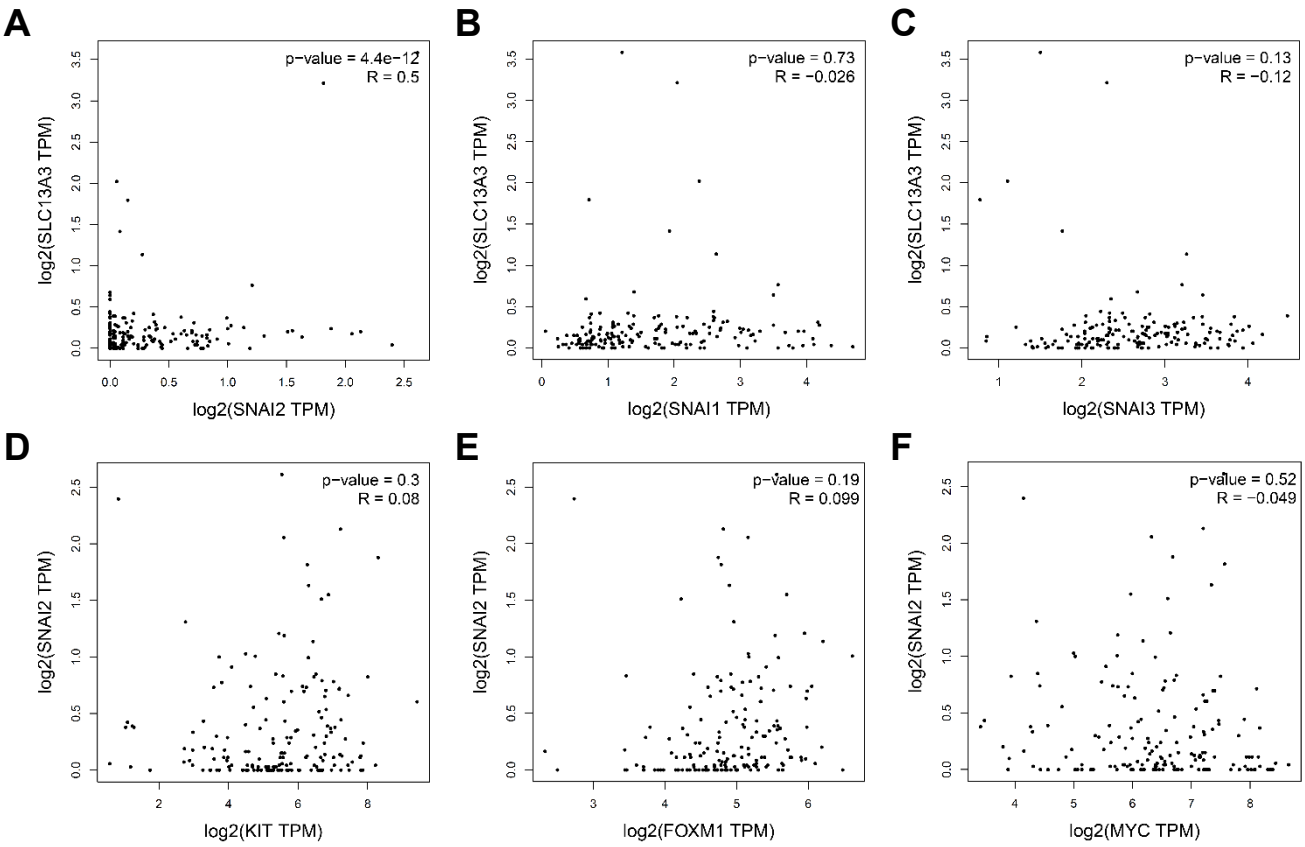
(**B**) The expression of SLUG between normal BM cells of healthy controls and FAB subtypes of AML patients. The data were obtained from a public microarray database (GSE3365, GSE12417 and GSE10358) (normal patient, n = 57; M0 patient n = 17; M1 patient n = 80; M2 patient n = 89; M3 patient n = 36; M4 patient n = 87; M5 patient n = 27).

(**C**) The expression of SLUG between normal GMPs and AML patients' L-GMPs (normal patient, n = 9; AML patient n =16).

(**D-I**) The proliferation/cell growth of human AML cells. Human AML cells were transduced with lentiviral particles and then performed puromycin selection. The cell number was counted at different time points (n = 3). (D) THP-1, (E) NOMOMAC-6, (F) NOMO-1, (G) MV4-11, (H) NB4, (I) Hu MA9.3 (n = 3).

(**J, K**) Colony-forming assay of human leukemic cells (n = 3).

Data are representative of three independent experiments. All data are represented as mean ± SD. Two-tailed Student's t-tests were used to assess statistical significance (* $P < 0.05$; ** $P < 0.01$).



Supplemental Figure 19. The analysis of gene correlation in samples from human patients with AML.

(**A-C**) Correlation analysis of expression of SLC13A3 with SLUG/SNIA2 (A), SNAI1 (B), SNAI3 (C), respectively. Expression levels were expressed in transcripts per million (TPM) (n = 173).

(**D-F**) Correlation analysis of expression SLUG/SNIA2 with KIT (A), FOXM1 (B), and c-MYC (C), respectively (n = 173).

Data are analyzed by online software GEPIA (http://gepia.cancer-pku.cn/detail.php). *P* values and *R* values are indicated.

Supplemental Table 3. List of primers for PCR

Primer	Sequence (5' to 3')	Application
SLUG-sh1-F1	ccggCAGCTGTAAATACTGTGACAActcgagTTGTCACAGTATTTACAGCTGTTTTTG	shRNA
SLUG-sh1-R1	aattcaaaaaCAGCTGTAAATACTGTGACAActcgagTTGTCACAGTATTTACAGCTG	shRNA
SLUG-sh2-F2	ccggGCCAAATCATTTCAACTGAAActcgagTTTCAGTTGAAATGATTTGGCTTTTTG	shRNA
SLUG-sh2-R2	aattcaaaaaGCCAAATCATTTCAACTGAAActcgagTTTCAGTTGAAATGATTTGGC	shRNA
Slc13a3-F1	ctgacAGATCTccATGGCGGCGCTGGCGGCG	PCR
Slc13a3-R1	CTGACgaatTCAGAAGGTTTGAACTGTGTTGTTGGTC	PCR
Elovl7-F1	ctgacGGATccATGGCGTTCAGTGATCTTACATCGAG	PCR
Elovl7-R1	CTGACgaattcTTAGTGGCGCTTGCTTTTGCAATTTC	PCR
Slc2a5-F1	ctgacGGATccATGGAGGAAAAACATCAAGAGGAGACAG	PCR
Slc2a5-R1	CTGACgaattcCTACTGCTCCAAGATGGCGTGTG	PCR
Gapdh-gF	CTTTGGCATTGTGGAAGGGCTCAT	PCR
Gapdh-gR	TGGAAGAGTGGGAGTTGCTGTTGA	PCR
Gadph-qF	CCGCCTGGAGAAACCTGCCAAG	PCR
Gadph-qR	TGCTGTAGCCGTATTCATTGTCATACCAG	PCR
Hprt-qF	CTCATGGACTGATTATGGACAGGAC	PCR
Hprt-qR	GCAGGTCAGCAAAGAACTTATAGCC	PCR
GADPH-qF	ATTGACCTCAACTACATGGTTTACATG	qPCR
GADPH-qR	TTGGAGGGATCTCGCTCCTGGAAG	qPCR
Tbrg1-qF	CCAGAAGCTCAAAACTGTGTCAATTACC	qPCR
Tbrg1-qR	AGGTCCAGGGAGCCTGGC	qPCR
Erdr1-qF	GGCACACACGGCAGGCAG	qPCR
Erdr1-qR	TGACCGGTGGACGCTGAC	qPCR
Slc13a3-qF	TCCTGGCAGAGCTGGCCATC	qPCR
Slc13a3-qR	AGGCCCGTCCGCACCATG	qPCR
Elovl7-qF	GGAGTCAAATTTGCTGCAGGTGG	qPCR
Elovl7-qR	GATAGTGACAAGAACAAACTGGACAAGC	qPCR
Slc2a5-qF	AGCTGCTGAGAGAGCCCTC	qPCR
Slc2a5-qR	GATCGGCGTAGTAGTAGATCGCG	qPCR
Slc13a3-gF	GCTTGGGCTAAATAAGAGCCTGTCCCAAC	qPCR
Slc13a3-gR	CGCGCCTCCTTGGTCTGGACA	PCR
Slug-102qF	GCGAACTGGACACACACACAGTTAT	qPCR
Slug-305qR	GCTGCCGACGATGTCCATACAGTAAT	qPCR
Slc13a3-PrF	tcgtGGTACcGACCAAACTCAGGTCACCAGGCCTG	PCR
Slc13a3-PrR	tgcgAAGCTTAAGGGACGGGGAGGAGCCATG	PCR
Slc13a3-gF2	TTGTGGCATCTGTCACTGAGAAGG	qPCR
Slc13a3-gR2	CACTCTGGACTCACGTGGGAAATG	qPCR

Supplemental Table 4. List of shRNAs used in the experiments

shNRA	Supplier	Catalog number
Slc13a3-shRNA #1	Sigma	TRCN0000070199
Slc13a3-shRNA #2	Sigma	TRCN0000070200
Slc13a3-shRNA #3	Sigma	TRCN0000070202
Slc13a3-shRNA #4	Sigma	TRCN0000416004

Supplemental Table 5. Gene expression profiles from microarray data analysis

Gene Symbol (or Genomic Position)	Fold change ($Slug^{+/+}$ vs. $Slug^{-/-}$)	ANOVA p-value
Mgl2	-6.06	0.030505
Mir101c	-5.05	0.047033
H2afy	-4.12	0.00429
Trim34a	-2.93	0.023388
Far2	-2.92	0.019632
C3	-2.84	0.034113
Olfr520	-2.74	0.039013
Tlr7	-2.72	0.02704
Mir3475	-2.63	0.035982
Olfr635	-2.61	0.001245
Tcp10c	-2.6	0.026439
Nrxn1	-2.6	0.040541
Vmn1r149	-2.52	0.005685
Spr-ps1	-2.49	0.036899
Igkv7-33	-2.48	0.009524
Dock1	-2.42	0.04346
Ptgs1	-2.4	0.002979
Gpr84	-2.28	0.048022
Gtsf1l	-2.28	0.025892
Tbrg1	-2.28	0.017372
Tdg	-2.25	0.004892
Olfr1512	-2.25	0.023997
Erdr1	-2.25	0.016088
Rmnd5a	-2.21	0.017495
Slc26a8	-2.17	0.049448
Vmn1r53	-2.17	0.026967
Lypd2	-2.1	0.02772
Rnase13	-2.08	0.044722
Slc13a3	-2.08	0.042847

Mir133a-1	-2.07	0.002533
Lcn2	-2.06	0.039996
Cpne5	-2.05	0.018697
Mpo	-2.04	0.018087
Wap	-2.02	0.031863
Vegfa	-2.01	0.046619
Snord91a	2.03	0.010122
Prg3	2.05	0.028375
Hist1h4m	2.08	0.029673
Ifi30	2.12	0.005741
Slc13a3	2.27	0.025726
Mir669a-2	2.28	0.044768
Mir677	2.29	0.043818
Depdc7	2.42	0.019115
Slc2a5	2.43	0.027002
Lpin2	2.47	0.00614
Trim30d	2.49	0.042937
Snord99	2.54	0.023828
Elvol7	2.92	0.043205
Cd2ap	3.12	0.028698
Dach1	3.28	0.043827
Aspa	5.42	0.03472

Supplemental Table 6. List of antibodies

Antibodies	Supplier	Catalog number
Mouse hematopoietic lineage biotin panel	eBioscience	88-7774-75
PE/Cy7 anti-mouse CD117(c-Kit)	Biolegend	105814
APC anti-mouse CD34 antibody	Biolegend	128611
APC/Cy7 anti-mouse CD16/32 antibody	Biolegend	101327
PerCP/Cy5.5 anti-mouse Ly-6G/Ly-6C (Gr-1)	Biolegend	108427
Anti-Flag Tag Monoclonal antibody	Thermo Scientific	MA1-91878
PE Annexin V	Biolegend	640907
Anti-SLC13A3 antibody	Sigma	AV41439