Table S1. Primer Sequences

Primers for genomic DNA	Sequences
SoNar-F	GGGGCGGCGTGATCGAGCACGTAG
SoNar-R	GCTTCTCGTTGGGGTCTTTGCTCAG
Actin-F	AGTCCCTCACCCTCCCAAAA
Actin-R	CAGACCTGGGCCATTCAGAAA
Primers for RT-PCR and qRT-PCR	**Sequences**
Ldha-F	TGTCTCCAGCAAAGACTACTGT
Ldha-R	GACTGTACTTGACAATGTTGGGA
Pkm2-F	ATTACCAGCGACCCCACAGA
Pkm2-R	ACTTGGTGAGCACTCCTGC
Glut1-F	CAGTTCGGCTATAACACTGGTG
Glut1-R	GCCCCCGACAGAGAAGATG
Glut2-F	TCAGAAGACAAGATCACCGGA
Glut2-R	GCTGGTGTGACTGTAAGTGGG
Glut3-F	ATGGGGACAACGAAGGTGAC
Glut3-R	GTCTCAGGTGCATTGATGACTC
Glut4-F	GTGACTGGAACACTGGTCCTA
Glut4-R	CCAGCCACGTTGCATTGTAG
Hk1-F	CGGAATGGGGAGCCTTTGG
Hk1-R	GCCTTCCTTATCCGTTTCAATGG
Pfkl-F	GGAGGCGAGAACATCAAGCC
Pfkl-R	CGGCCTTCCCTCGTAGTGA
Pkm2-F	TGTGGTCCGAGTTGGTATCTT
Pkm2-R	GCACTTCCAATCACTGTGCC
Gapdh-F	AGGTCGGTGTGAACGGATTTG
Gapdh-R	TGTAGACCATGTAGTTGAGGTCA
Mct1-F	TGTTAGTCGGAGCCTTCATTTC
Mct1-R	CACTGGTCGTTGCACTGAATA
Mct2-F	GCTGGGTCGTAGTCTGTGC
Mct2-R	ATCCAAGCGATCTGACTGGAG
Mct3-F	TCACGGGTTTCTCCTACGC
Mct3-R	GCCAAAGCGGTTCACACAC
Mct5-F	CCTTACACCAAACCCCTTGATG
Mct5-R	CCAATCCAACCAATTTGCTCTG
Mpc1-F	ATGAGTACGCACTTCTGGGG
Mpc1-R	CGCCCACTGATAATCTCTGGA
Mpc2-F	TACCACCGACTCATGGATAAAGT
Mpc2-R	CACACACCAATCCCCATTTCA
Pdhx-F	GCTTCACTGTAACCAGCCG
Pdhx-R	CCCTTGCTCCATCGTAGGAGA
Fh1-F	GAATGGCAAGCCAAAATTCCTT
Fh1-R	CGTTCCGTAGCACCTCCAATCTT

Idh1-F	ATGCAAGGAGATGAAATGACACG
Idh1-R	GCATCACGATTCTCTATGCCTAA
Idh2-F	GGAGAAGCCGGTAGTGGAGAT
Idh2-R	GGTCTGGTCACGGTTTGGAA
Idh3a-F	TGGGTGTCCAAGGTCTCTC
Idh3a-R	CTCCCACTGAATAGGTGCTTTG
Idh3b-F	TGGAGAGGTCTCGGAACATCT
Idh3b-R	AGCCTTGAACACTTCCTTGAC
Idh3g-F	GGTGCTGCAAAGGCAATGC
Idh3g-R	TATGCCGCCCACCATACTTAG
Aco2-F	ATCGAGCGGGGAAAGACATAC
Aco2-R	TGATGGTACAGCCACCTTAGG
Atp5l-F	GAGAAGGCACCGTCGATGG
Atp5l-R	ACACTCTGAATAGCTGTAGGGAT
Atp5o-F	TCTCGACAGGTTCGGAGCTT
Atp5o-R	AGAGTACAGGGCGGTTGCATA
Cox6b1-F	ACTACCTGGACTTCCACCG
Cox6b1-R	ACCCATGACACGGGACAGA
Cox18-F	GGCCGCCTATCAGCACTAC
Cox18-R	TGAGATAAGTCTCCGCATGTTCT
Ndufb5-F	CAAGAGACTGTTTGTCGTCAAGC
Ndufb5-R	TGTTCACCAGTGTTATGCCAAT
Gdpd-F	CACAGTGGACGACATCCGAAA
Gdpd-R	AGCTACATAGGAATTACGGGCAA
Pgd-F	TGAAGGGTCCTAAGGTGGTCC
Pgd-R	CCGCCATAATTGAGGGTCCAG
Gls-F	TTCGCCCTCGGAGATCCTAC
Gls-R	CCAAGCTAGGTAACAGACCCT
Gdh-F	CCCAACTTCTTCAAGATGGTGG
Gdh-R	AGAGGCTCAACACATGGTTGC
Phgdh-F	ATGGCCTTCGCAAATCTGC
Phgdh-R	AGTTCAGCTATCAGCTCCTCC
Actin-F	GGCTGTATTCCCCTCCATCG
Actin-R	CCAGTTGGTAACAATGCCATGT
SoNar-F	GGGGCGGCGTGATCGAGCACGTAG
SoNar-R	GCTTCTCGTTGGGGTCTTTGCTCAG
mt-ND4-F	GGAACCAAACTGAACGCCTA
mt-ND4-R	ATGAGGGCAATTAGCAGTGG
B2m-F	TCATTAGGGAGGAGCCAATG
B2m-R	ATCCCCTTTCGTTTTTGCTT
Mdh1-F	AGATTGCCTTCAAAGACCTGG
Mdh1-R	GCAGTTCGTATTGGCTGGGT
Mdh2-F	TTGGGCAACCCCTTTCACTC
Mdh2-R	GCCTTTCACATTTGCTCTGGTC

SoNar-F	CGGCTGGGCAGCGCCCTGGC
SoNar-R	GCCGGGCACCGCTGGGGCA
shRNA for Mdh1 and Mdh2	**Target sequences**
shMdh1#1	GCCCATCATTCTTGTGCTGTT
shMdh1#2	CTTGGAGAAATACGCCAAGAA
shMdh1#3	CCAAGGTGAAACTGCAAGGAA
shMdh2#1	GCAGAGCTAAAGGGTTTGGAT
shMdh2#2	CGGAATGCACTTACTTCTCTA
shMdh2#3	CGGTGTGTACAACCCTAACAA
ChIP for Mdh1	**Sequences**
ChIP-Mdh1-F	CTTCTTGGCTTTGTGAGGCC
ChIP-Mdh1-R	TGGTGGTCTGGTGAGTAATT
MSP PCR primer for Mdh1	**Sequences**
MDH1-MSP-1-F	GTTTTTGATATTAATAGGGGATTT
MDH1-MSP-1-R	CCAAAAACTTATAAAACTATATTCTCAC

Figure S1

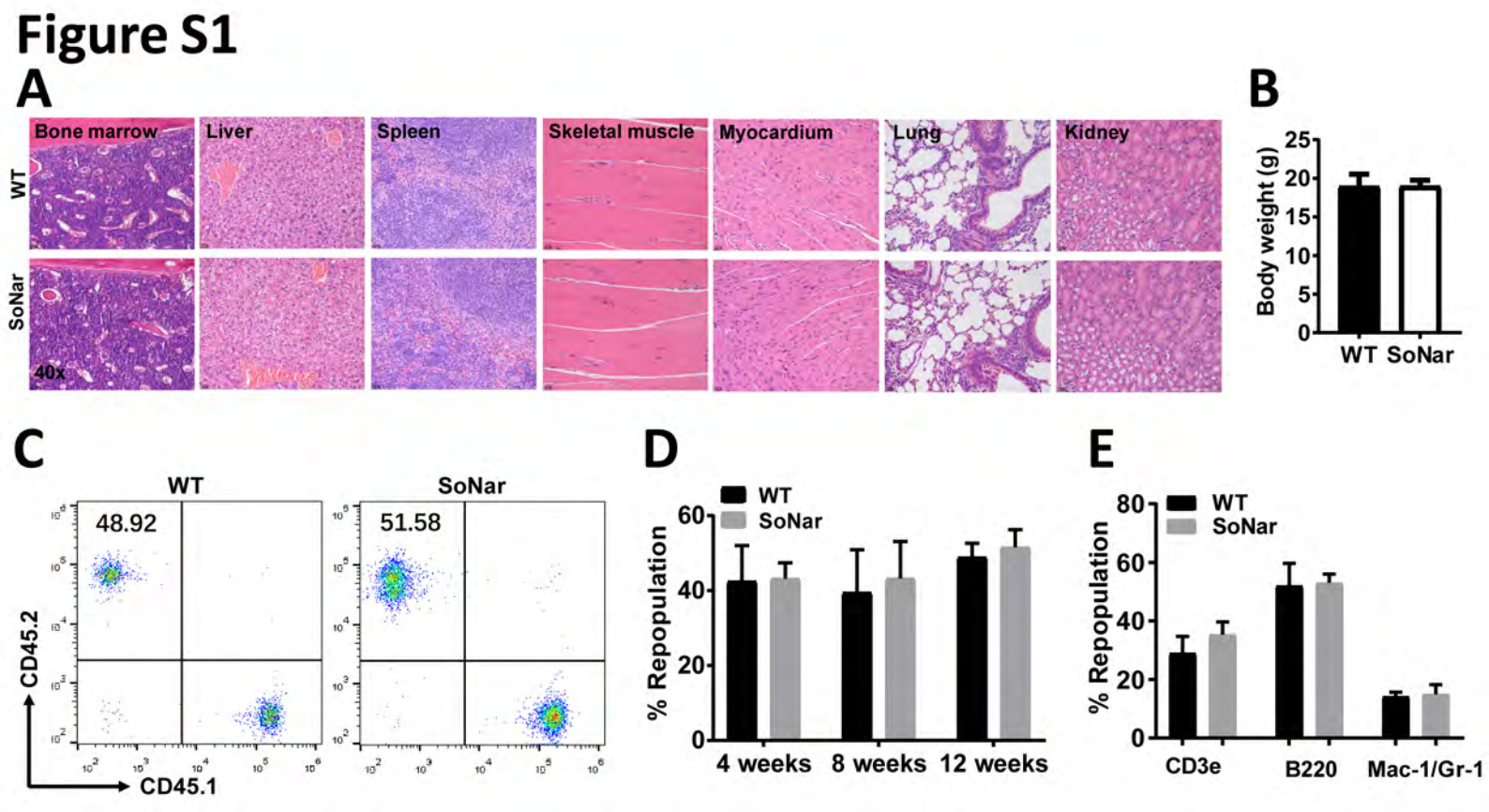

A
Bone marrow
Liver
Spleen
Skeletal muscle
Myocardium
Lung
Kidney
WT
SoNar
40x
B
Body weight (g)
25
20
15
10
5
0
WT
SoNar
C
WT
SoNar
48.92
51.58
CD45.2
CD45.1
D
WT
SoNar
% Repopulation
60
40
20
0
4 weeks
8 weeks
12 weeks
E
WT
SoNar
% Repopulation
80
60
40
20
0
CD3e
B220
Mac-1/Gr-1

Figure S1, related to Figure 1. (**A**) Pathologic status was evaluated in different tissues of WT and SoNar transgenic mice by hematoxylin/eosin staining. Scale bar: 50 μm. (**B**) Body weight was examined in both 6-8 weeks WT and SoNar transgenic mice (n=10). (**C**) Representative flow cytometric plots of the frequencies of repopulated cells in the peripheral blood of recipients transplanted with WT and SoNar transgenic adult-HSC donor (CD45.2) or competitive cells (CD45.1). (**D**) Quantification of data of the repopulated donor cells at 4, 8 and 12 weeks post-transplant in panel C (n=5). (**E**) Multilineage contribution of donor cells in the primary recipients at 12 weeks post-transplant in panel D (n=5). Data are represented as mean ± SEM. Student's two-tailed unpaired t test (B) or two-way ANOVA with Sidak's multiple comparison test (D and E) was used for the comparison of statistical significance.

Figure S2

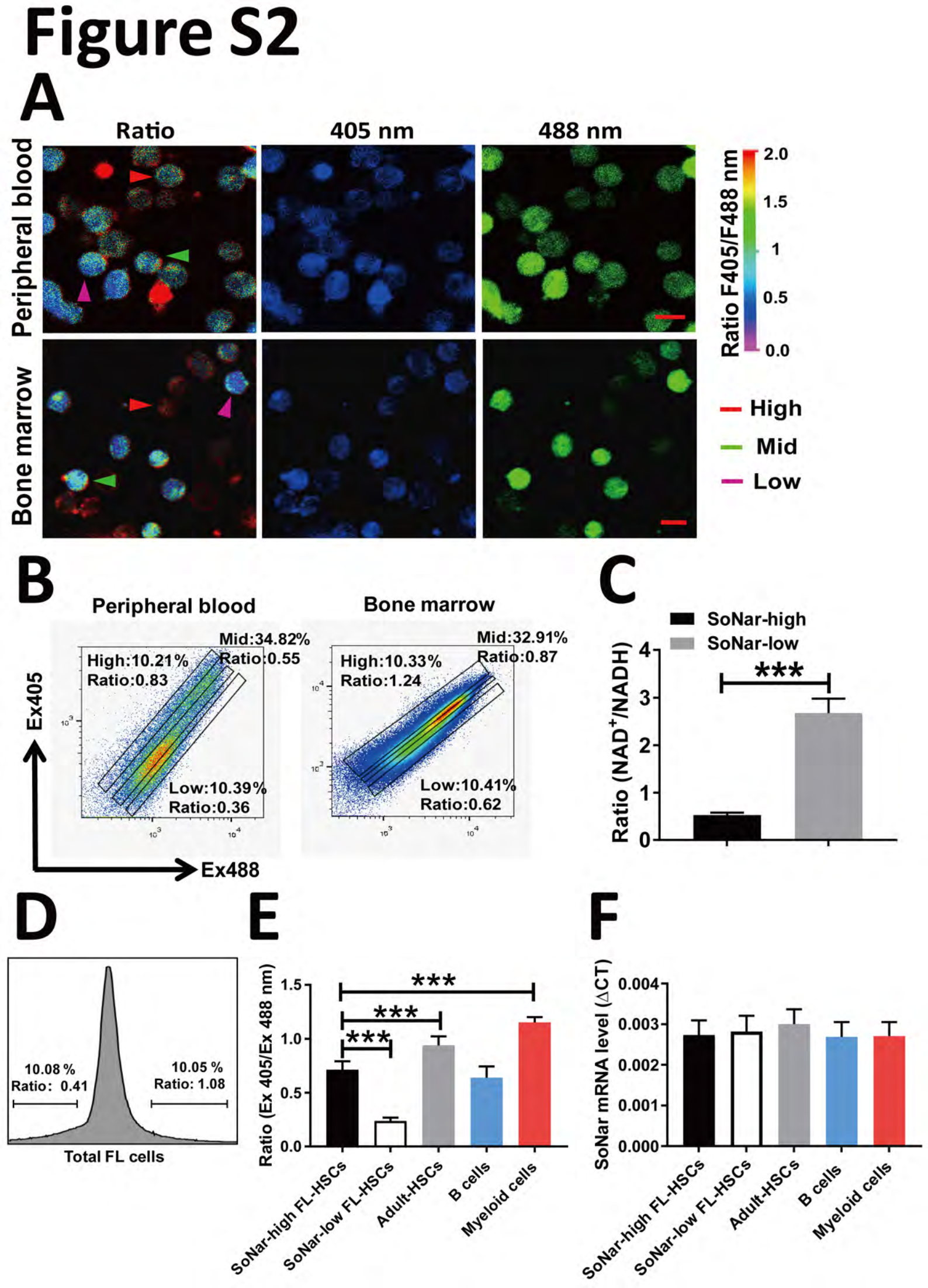

A
Ratio
405 nm
488 nm
Peripheral blood
Bone marrow
Ratio F405/F488 nm
2.0
1.5
1
0.5
0.0
High
Mid
Low
B
Peripheral blood
Bone marrow
Mid:34.82%
Ratio:0.55
High:10.21%
Ratio:0.83
Low:10.39%
Ratio:0.36
Mid:32.91%
Ratio:0.87
High:10.33%
Ratio:1.24
Low:10.41%
Ratio:0.62
Ex405
Ex488
C
SoNar-high
SoNar-low
***
Ratio (NAD+/NADH)
D
10.08 %
Ratio: 0.41
10.05 %
Ratio: 1.08
Total FL cells
E
Ratio (Ex 405/Ex 488 nm)
***
***
***
SoNar-high FL-HSCs
SoNar-low FL-HSCs
Adult-HSCs
B cells
Myeloid cells
F
SoNar mRNA level (ΔCT)
SoNar-high FL-HSCs
SoNar-low FL-HSCs
Adult-HSCs
B cells
Myeloid cells

Figure S2, related to Figure 2. (**A**) Peripheral blood and bone marrow cells from SoNar transgenic mice were evaluated for the ratios of SoNar fluorescence with excitation at 405 and 488 nm by confocal microscopy, and representative images are shown. Scale bar: 10 μm. (**B**) Representative flow cytometric analyses of the ratios of SoNar fluorescence in peripheral blood and bone marrow $CD45^+$ hematopoietic cells. Frequencies and Ratios of SoNar-high, -middle (mid) and -low FL hematopoietic cells are indicated. (**C**) NAD^+/NADH levels were determined in SoNar-high and -low FL hematopoietic cells by using a commercial available NADH/NAD^+ assay kit and the ratio was calculated (n=5). (**D**) Representative flow cytometric analyses (histogram) of ratios of SoNar fluorescence (F405/F488 nm) in total FL hematopoietic cells. (**E-F**) The ratios of SoNar fluorescence (E) and relative SoNar mRNA expression levels (F) were determined in FL-high-HSCs, FL-low-HSCs, adult-HSCs, differentiated B cells and myeloid cells in the BM (n=3-5). Data are represented as mean ± SEM. Student's two-tailed unpaired t test (C) or and one-way ANOVA with Tukey's multiple comparison test (E and F) were used for the comparison of statistical significance. ***, $p<0.001$.

Figure S3

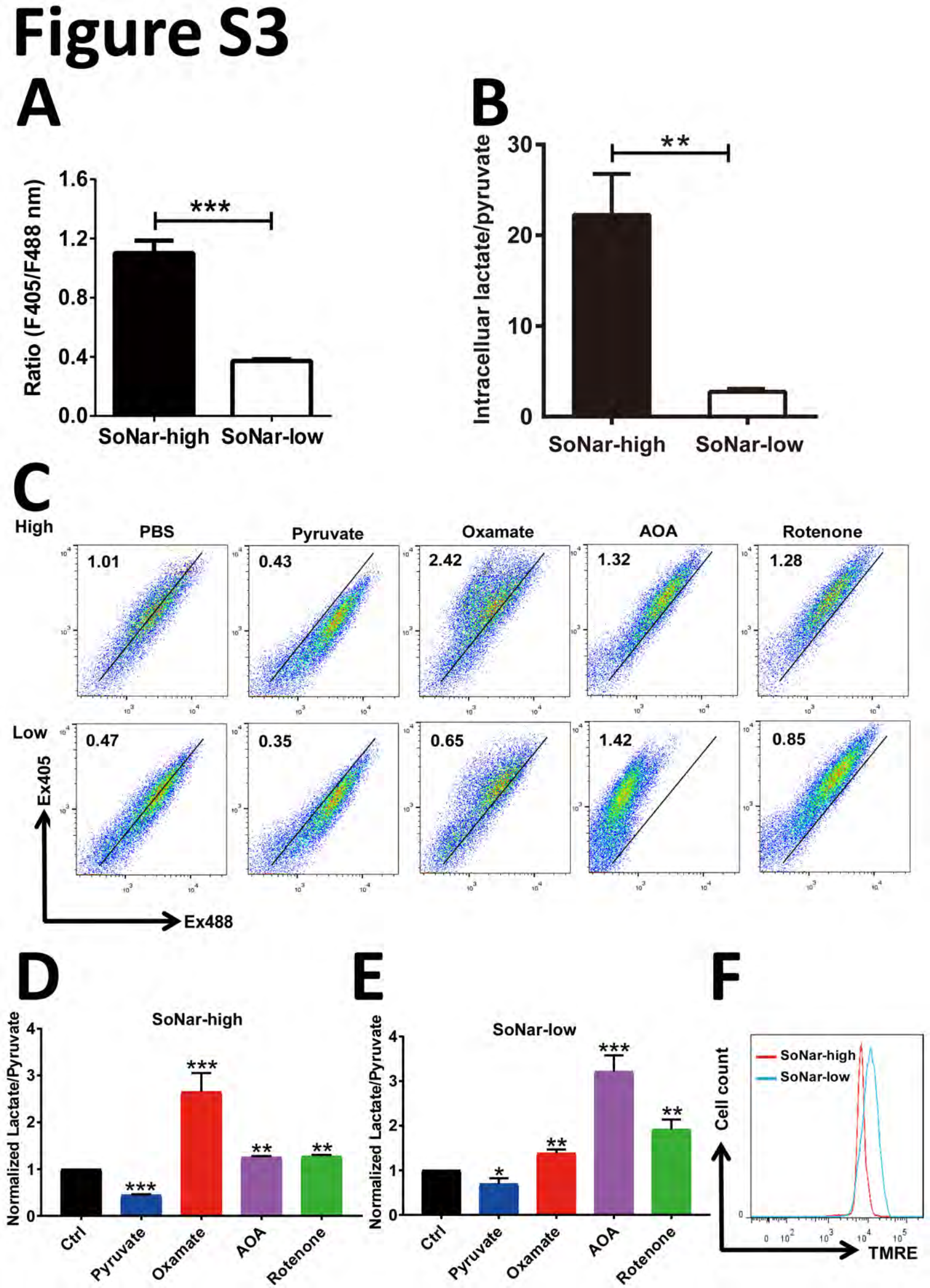
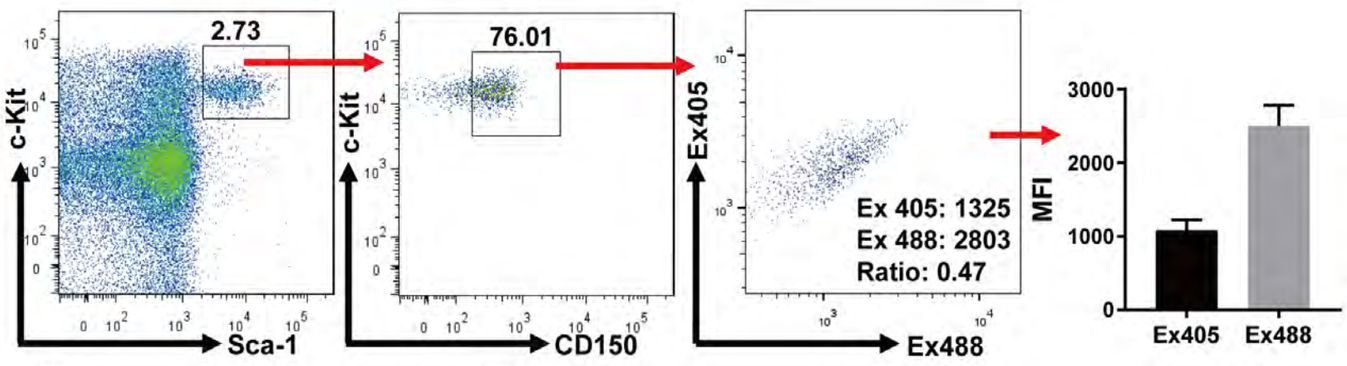
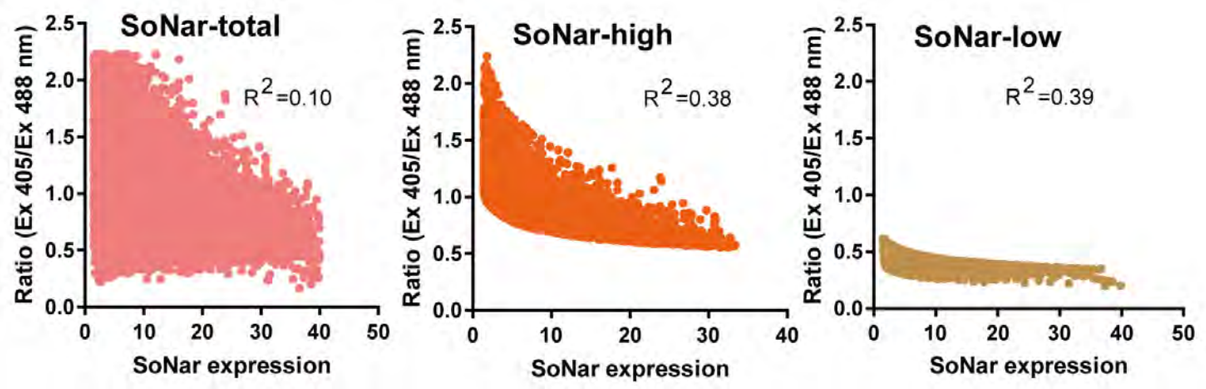
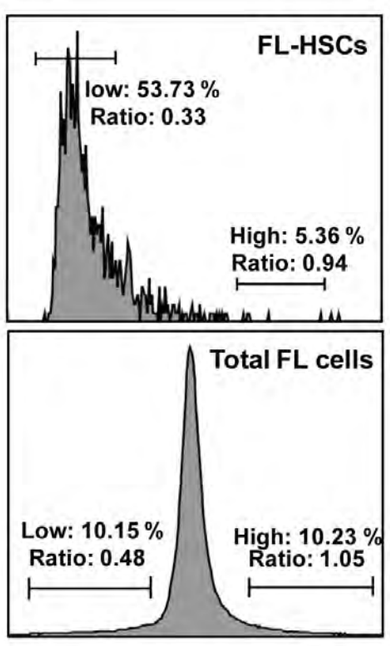

A
Ratio (F405/F488 nm)
1.6
1.2
0.8
0.4
0.0
***
SoNar-high
SoNar-low
B
Intracelluar lactate/pyruvate
30
20
10
0
**
SoNar-high
SoNar-low
C
High
PBS
Pyruvate
Oxamate
AOA
Rotenone
1.01
0.43
2.42
1.32
1.28
Low
0.47
0.35
0.65
1.42
0.85
Ex405
Ex488
D
SoNar-high
Normalized Lactate/Pyruvate
Ctrl
Pyruvate
Oxamate
AOA
Rotenone
E
SoNar-low
Normalized Lactate/Pyruvate
F
Cell count
SoNar-high
SoNar-low
TMRE

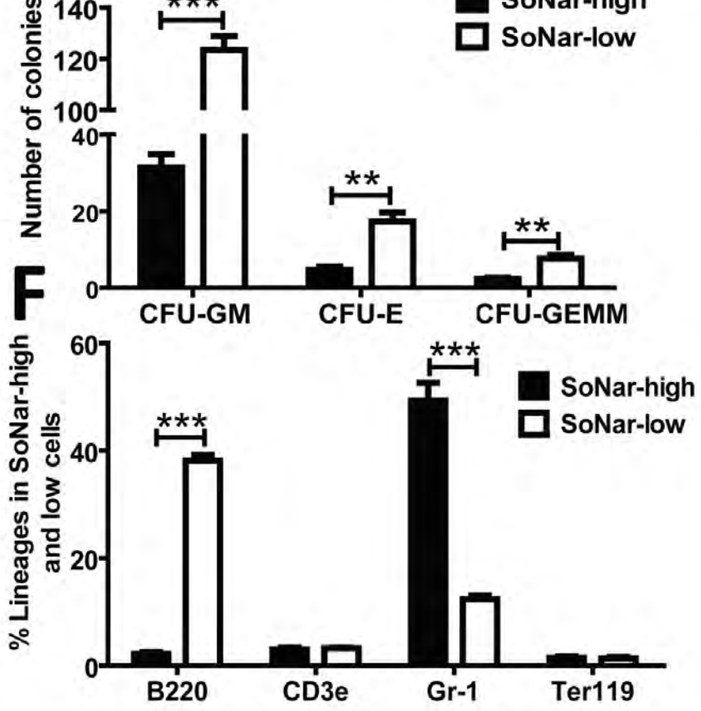
Figure S3, related to Figure 3. (**A**) Quantification of the ratios of SoNar fluorescence (F405/F488 nm) of $CD45^+$ SoNar-high and -low FL hematopoietic cells in Figure 3A as measured by flow cytometric analysis (n=6) (**B**) Intracellular lactate and pyruvate in $CD45^+$ SoNar-high and -low FL hematopoietic cells were measured and normalized to pyruvate (n=3). (**C**) Representative flow cytometric analyses of the ratios of SoNar fluorescence in $CD45^+$ SoNar-high and -low FL hematopoietic cells upon PBS, pyruvate, oxamate, AOA or rotenone treatment. (**D** and **E**) Intracellular lactate and pyruvate in $CD45^+$ SoNar-high (D) and -low FL hematopoietic cells (E) were measured and normalized to PBS upon pyruvate, oxamate, AOA, or rotenone incubation. (**F**) Mitochondrial membrane potential was evaluated in $CD45^+$ SoNar-high and -low FL hematopoietic cells by staining with TMRE probe. Data are represented as mean ± SEM. Student's two-tailed unpaired t test (A and B), and one-way ANOVA with Tukey's multiple comparison test (D and E) were used for the comparison of statistical significance. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$.

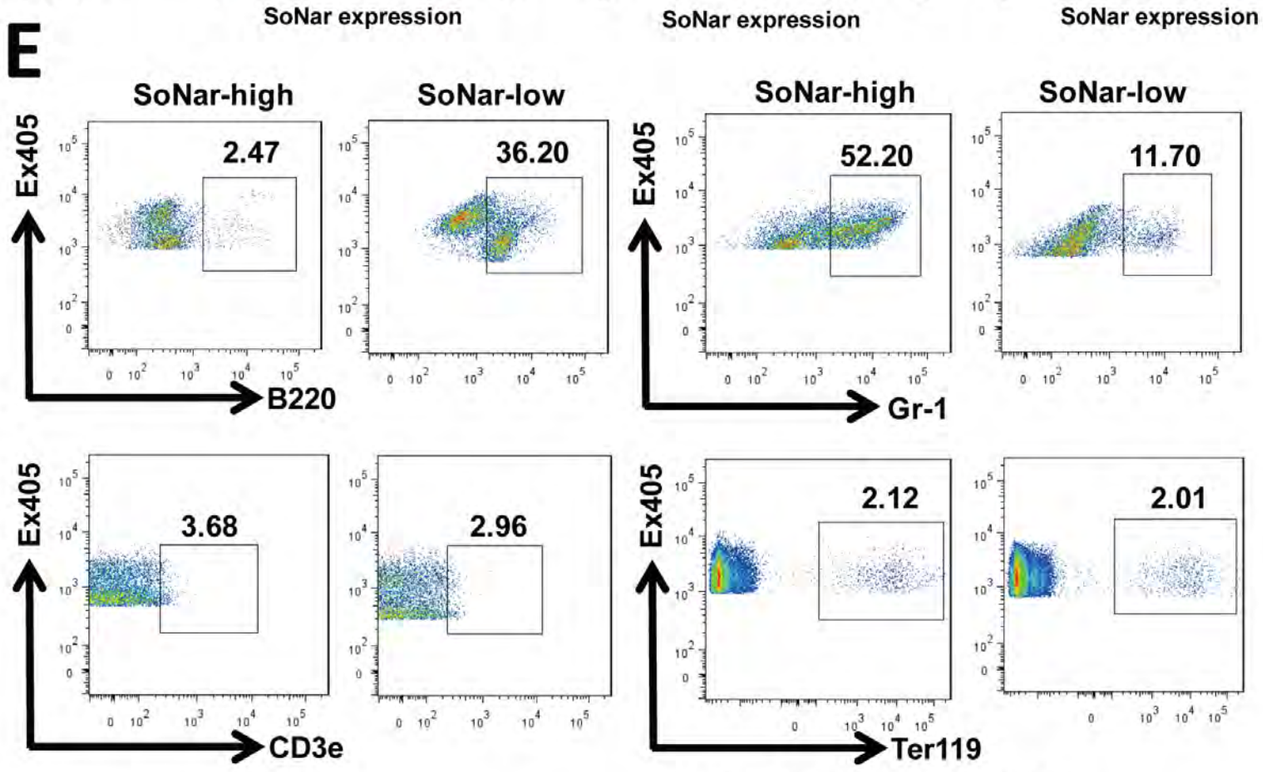
Figure S4

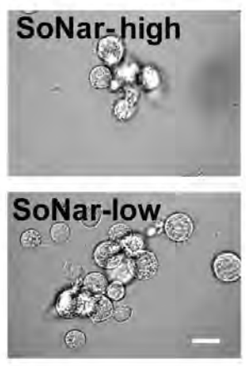

A
2.73
76.01
c-Kit
Sca-1
CD150
Ex405
Ex488
Ex 405: 1325
Ex 488: 2803
Ratio: 0.47
MFI
Ex405
Ex488

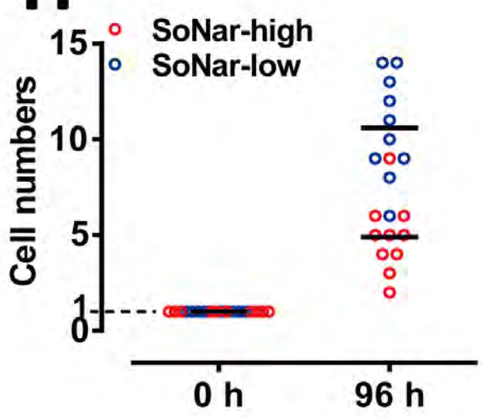

B
SoNar-total
SoNar-high
SoNar-low
R2=0.10
R2=0.38
R2=0.39
Ratio (Ex 405/Ex 488 nm)
SoNar expression

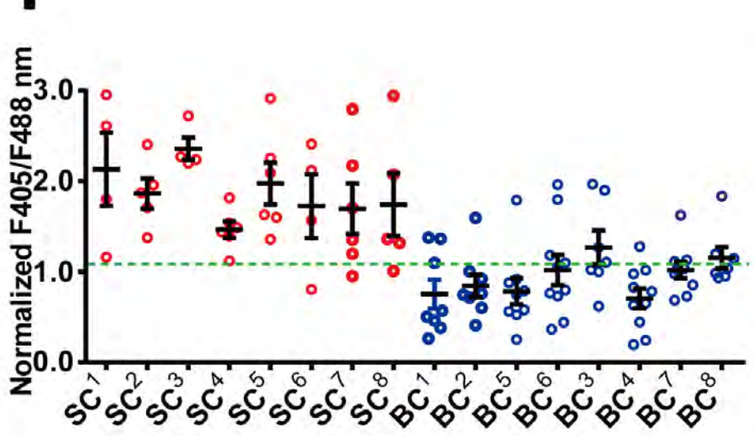

C
FL-HSCs
low: 53.73 %
Ratio: 0.33
High: 5.36 %
Ratio: 0.94
Total FL cells
Low: 10.15 %
Ratio: 0.48
High: 10.23 %
Ratio: 1.05

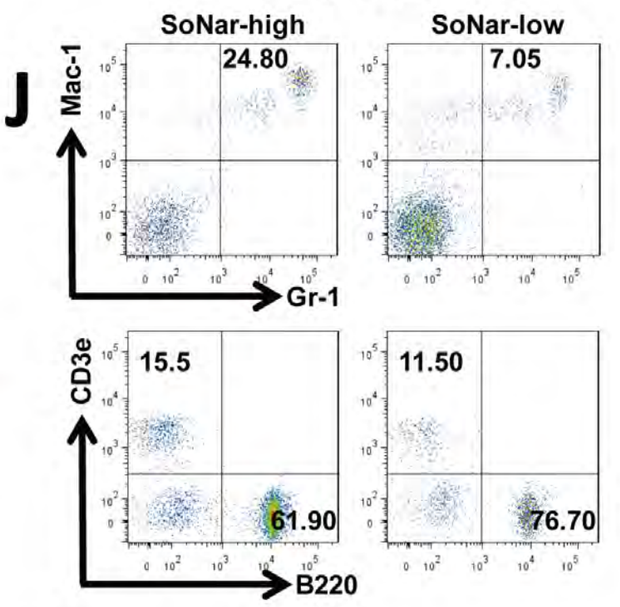

D
SoNar-high
SoNar-low
Number of colonies
CFU-GM
CFU-E
CFU-GEMM
% Lineages in SoNar-high and low cells
B220
CD3e
Gr-1
Ter119

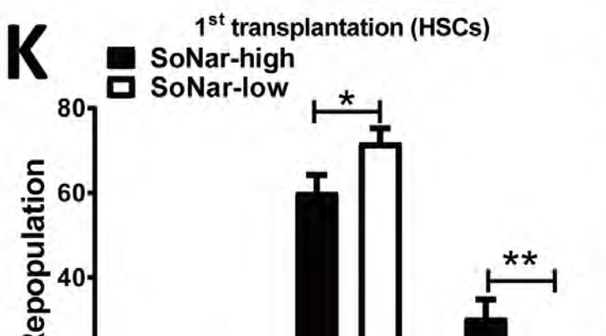

E
SoNar-high
SoNar-low
Ex405
B220
CD3e
Gr-1
Ter119
2.47
36.20
52.20
11.70
3.68
2.96
2.12
2.01

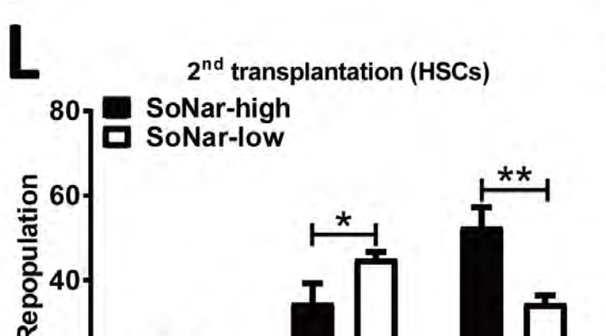

G
SoNar-high
SoNar-low

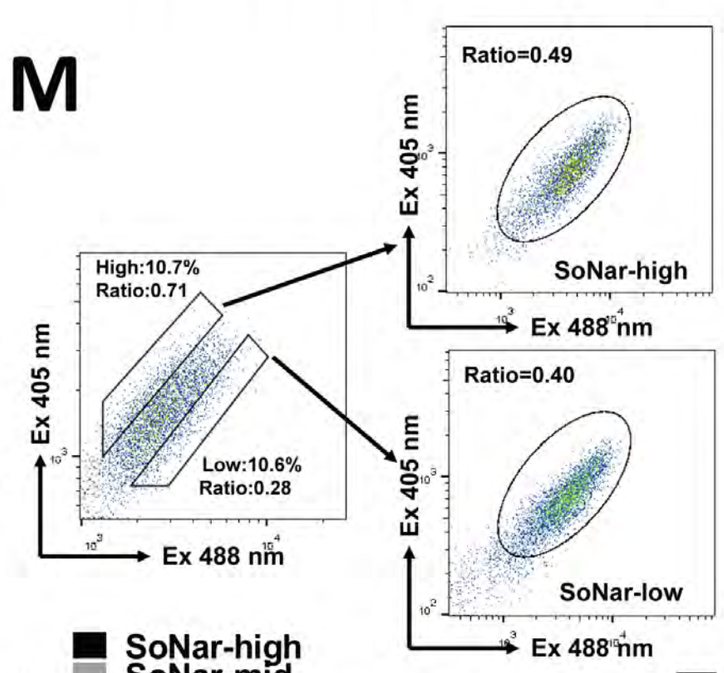

H
SoNar-high
SoNar-low
Cell numbers
0 h
96 h

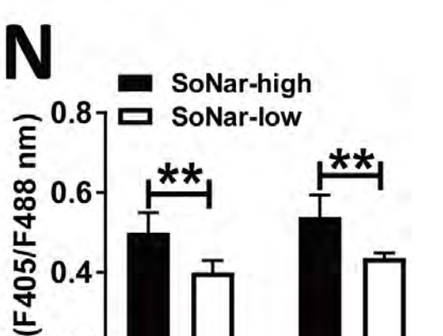

I
Normalized F405/F488 nm
SC1 SC2 SC3 SC4 SC5 SC6 SC7 SC8 BC1 BC2 BC5 BC6 BC3 BC4 BC7 BC8

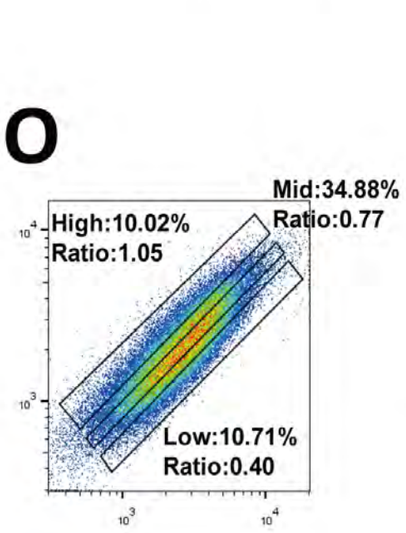

J
SoNar-high
SoNar-low
Mac-1
Gr-1
CD3e
B220
24.80
7.05
15.5
11.50
61.90
76.70

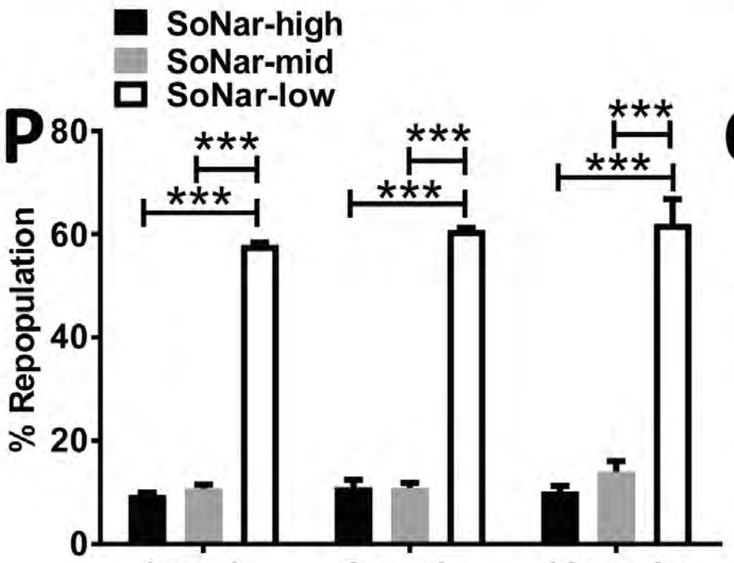

K
1st transplantation (HSCs)
SoNar-high
SoNar-low
% Repopulation
CD3e
B220
Mac-1/Gr-1

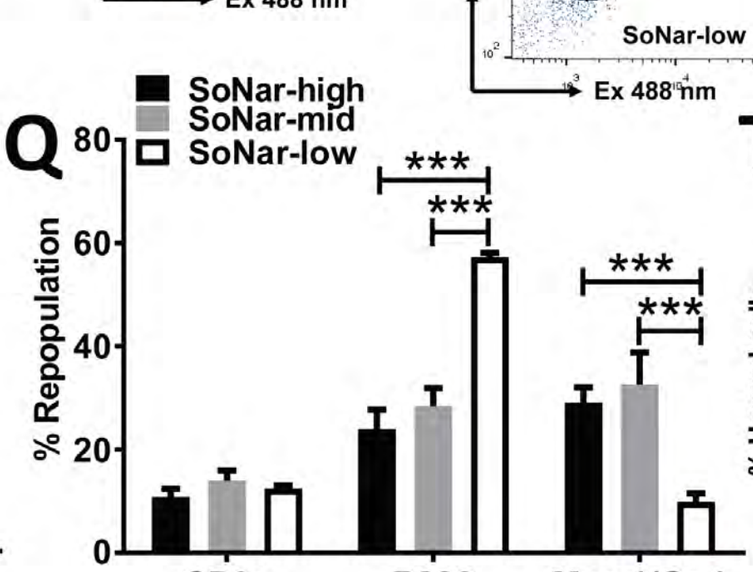

L
2nd transplantation (HSCs)
SoNar-high
SoNar-low
% Repopulation
CD3e
B220
Mac-1/Gr-1

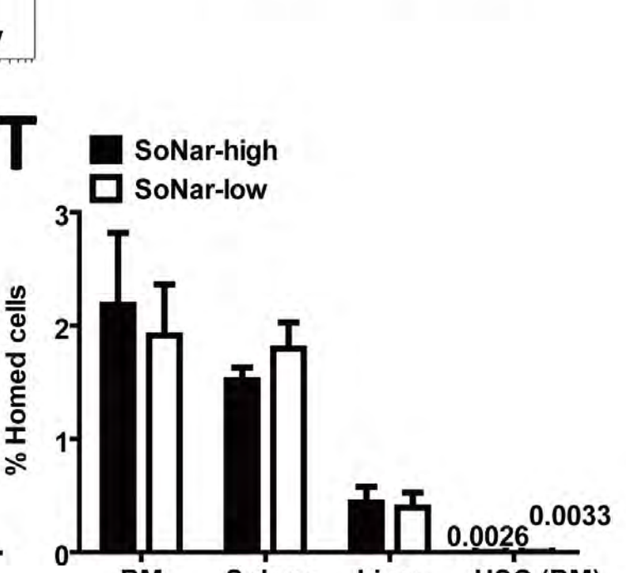

M
Ratio=0.49
High:10.7%
Ratio:0.71
Low:10.6%
Ratio:0.28
Ratio=0.40
Ex 405 nm
Ex 488 nm
SoNar-high
SoNar-low

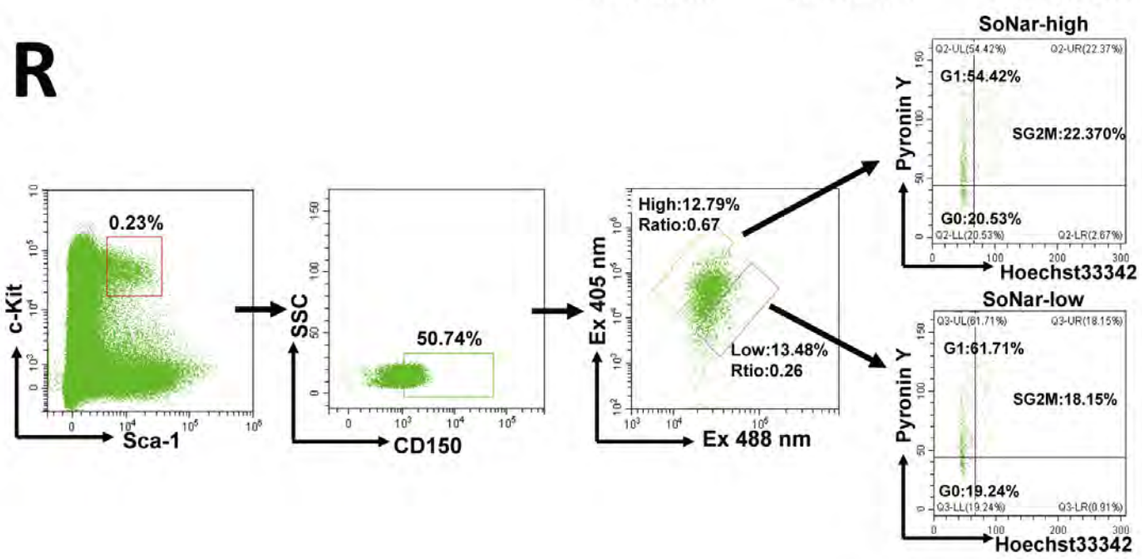

N
SoNar-high
SoNar-low
Ratio (F405/F488 nm)
8 weeks
12 weeks

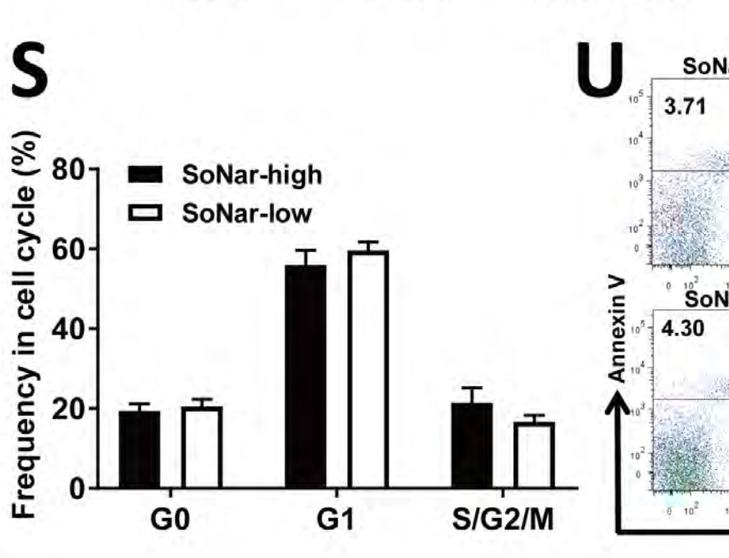

O
High:10.02%
Ratio:1.05
Mid:34.88%
Ratio:0.77
Low:10.71%
Ratio:0.40


P
SoNar-high
SoNar-mid
SoNar-low
% Repopulation
4 weeks
8 weeks
16 weeks


Q
SoNar-high
SoNar-mid
SoNar-low
% Repopulation
CD3e
B220
Mac-1/Gr-1


T
SoNar-high
SoNar-low
% Homed cells
BM
Spleen
Liver
HSC (BM)
0.0026
0.0033


R
0.23%
50.74%
High:12.79%
Ratio:0.67
Low:13.48%
Rtio:0.26
SoNar-high
SoNar-low
G1:54.42%
SG2M:22.370%
G0:20.53%
G1:61.71%
SG2M:18.15%
G0:19.24%
Pyronin Y
Hoechst33342


S
SoNar-high
SoNar-low
Frequency in cell cycle (%)
G0
G1
S/G2/M

U
SoNar-high
SoNar-low
3.71
0.38
4.30
0.27
Annexin V
PI

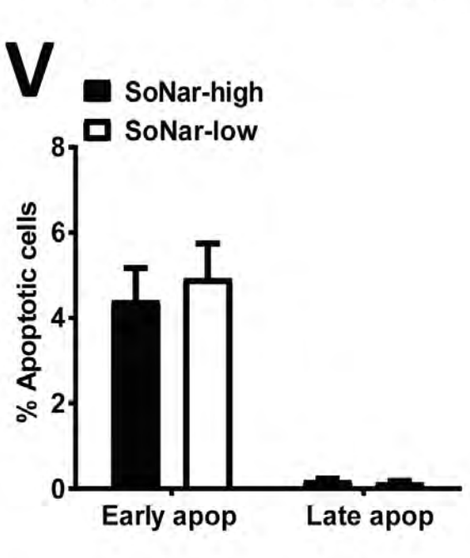
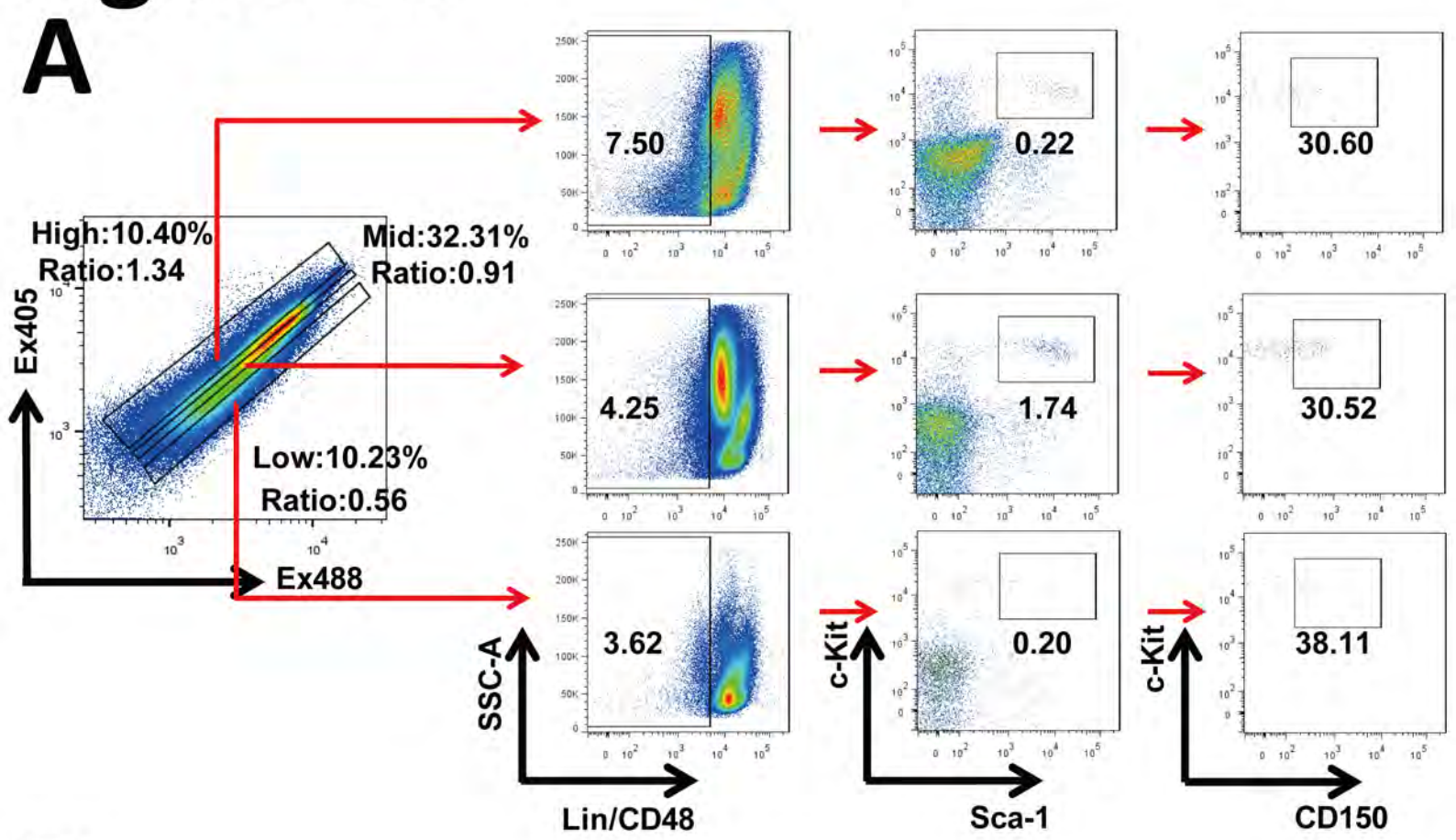
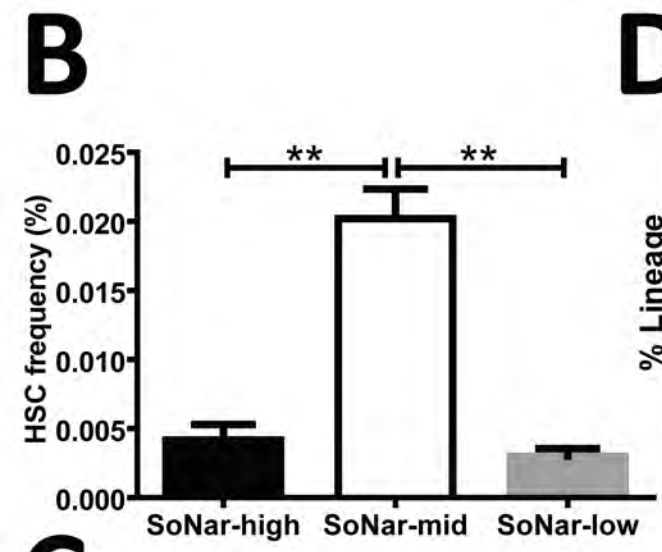

V
SoNar-high
SoNar-low
% Apoptotic cells
Early apop
Late apop

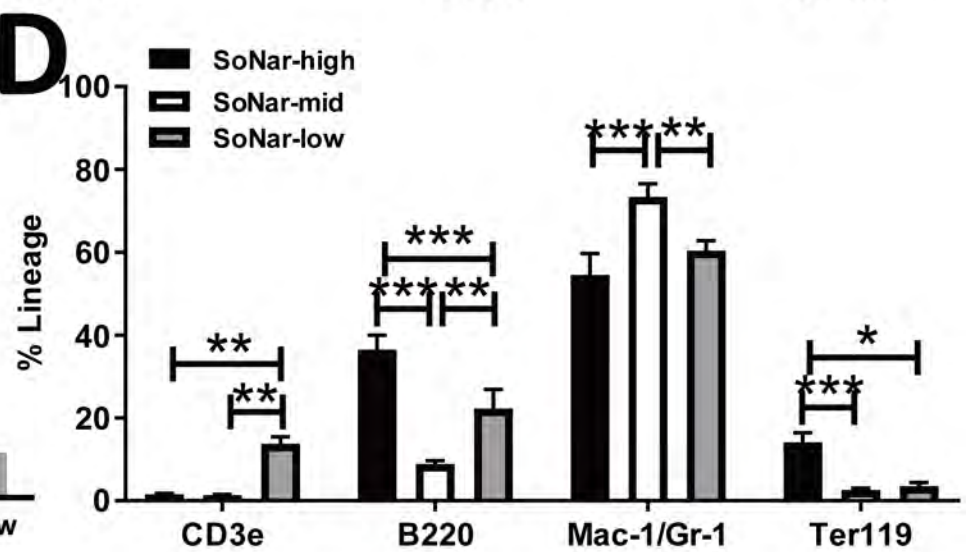
Figure S4, related to Figure 4. (**A**) Immunophenotypic $Lin^{-}Sca\text{-}1^{+}c\text{-}Kit^{+}CD150^{+}CD48^{-}$ FL-HSCs were gated and subjected for the analysis of the ratios of SoNar fluorescence. The mean fluorescence intensity (MFI) at excitation of 405 and 488 were quantified (n=5). (**B**) The coefficient of determination between SoNar fluorescence ratios (F405/F488) and its expression levels in total SoNar FL hematopoietic cells (Left), SoNar-high cells (Middle), and SoNar-low cells (Right). Data are from panel Figure 4A. SoNar expression levels are calculated using weighted average fluorescence excited at 405 nm and 488nm. Approximately 16,000 FL hematopoietic cells are used for the analysis. (**C**) Representative flow cytometric analyses (histogram) of ratios of SoNar fluorescence (F405/F488 nm) in total $CD45^{+}$ FL hematopoietic cells and FL-HSCs. (**D**) Frequencies of functional progenitor cells, as indicated as CFU-GEMM, CFU-GM, and CFU-E, were evaluated in $CD45^{+}$ SoNar-high and -low FL hematopoietic cells using the methylcellulose medium M3434 (n=3). (**E**) Representative flow cytometric analyses of percentages of B cells ($B220^{+}$), myeloid cells ($Gr\text{-}1^{+}$), T cells ($CD3e^{+}$), and erythroid cells ($Ter119^{+}$) in $CD45^{+}$ SoNar-high and -low FL cells. (**F**) Quantification of percentages of lineage cells in panel E (n=5). (**G** and **H**) Representative images of the colonies (G) or total cell numbers (H) derived from a single $CD45^{+}$ SoNar-high and -low FL hematopoietic cell (E12.5) 96 h after culture. A total of 10 cells were cultured (n=3). Scale bar: 10 μm. (**I**) The overall ratios of SoNar fluorescence were evaluated in big colonies (BC) and small colonies (SC) derived from a single cell 96 h after culture (n=3). (**J**) Representative flow cytometric analyses of frequencies of donor derived myeloid cells ($Mac\text{-}1^{+}Gr\text{-}1^{+}$), B cells ($B220^{+}$), and T cells ($CD3e^{+}$) in the primary

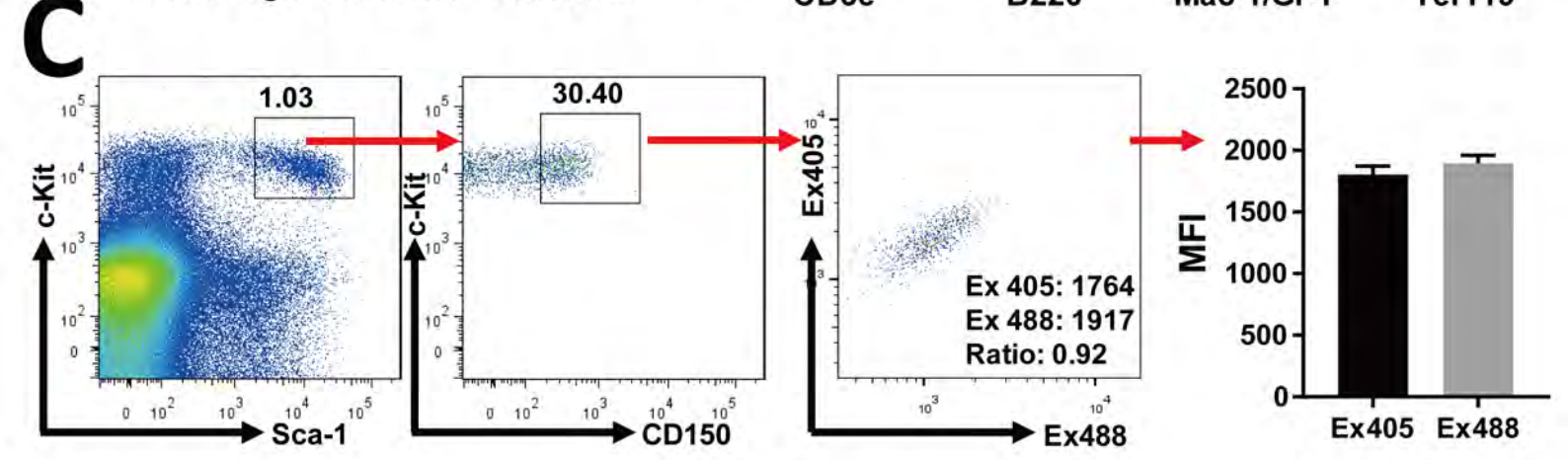
transplantation. (**K** and **L**) Multilineage contribution of donor cells in the primary or secondary recipients receiving SoNar-high or SoNar-low FL-HSCs at 16 weeks post-transplant (n=5). (**M**-**N**) Represetative flow cytometric analyses of the ratios of SoNar fluorescence from FL-high and -low HSCs and their repopulated hematopoietic cells in the peripheral blood of the recipient mice (M). Quantification data of the SoNar ratios in repopulated cells in panel M (N, n=5). (**O**-**Q**) $CD45^+$ SoNar-high, -middle (mid) and -low FL hematopoietic cells were sorted for the competitive transplantation (O), followed by the analysis for the repopulated donor cells in recipients at indicated time points (P). Multilineage contribution of donor cells were determined at 16 weeks post-transplant (Q, n=5). (**R**-**S**) Representative flow cytometric analyses of the cell cycle status in immunophenotypic $Lin^-Sca\text{-}1^+c\text{-}Kit^+CD150^+CD48^-$ SoNar-high and -low FL-HSCs (R). Quantification data of the frequencies of G0, G1 and S/G2/M phases in panel R are shown (S, n=4). (**T**) Frequencies of $SoNar^+$ cells in the BM, spleen and liver, and HSCs ($SoNar^+$ $Lin^-Sca\text{-}1^+c\text{-}Kit^+CD150^+CD48^-$ cells) in the BM were determined in recipient mice 16 h after receiving $CD45^+$ SoNar-high and -low FL hematopoietic cells (n=5). (**U**) Representative flow cytometric analyses of percentages of early and late apoptotic cells in $CD45^+$ SoNar-high and -low FL hematopoietic cell populations. (**V**) Quantification data of apoptosis in $CD45^+$ SoNar-high and -low FL hematopoietic cells in panel U. Early and late apoptotic cells were defined as Annexin V^+PI^- and Annexin V^+PI^+ cells, respectively (n=5). Data are represented as mean ± SEM. Two-way ANOVA with Sidak's multiple comparison test was used for the comparison of statistical significance. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$.

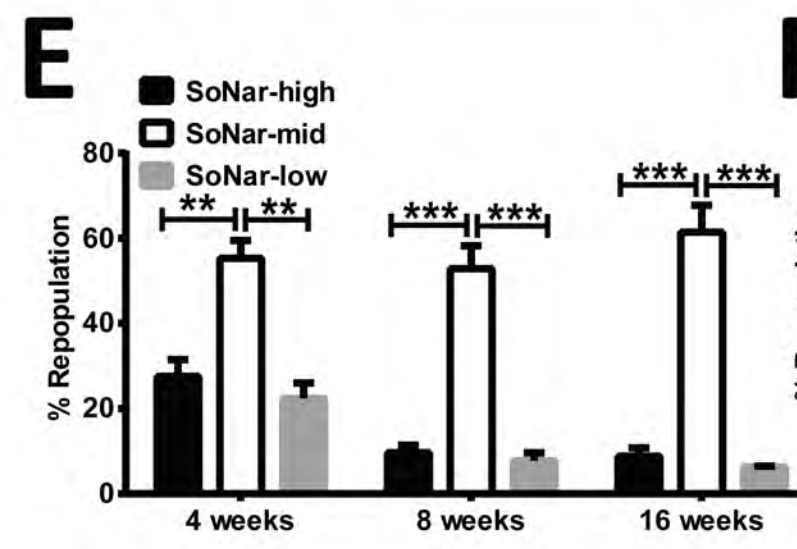
Figure S5

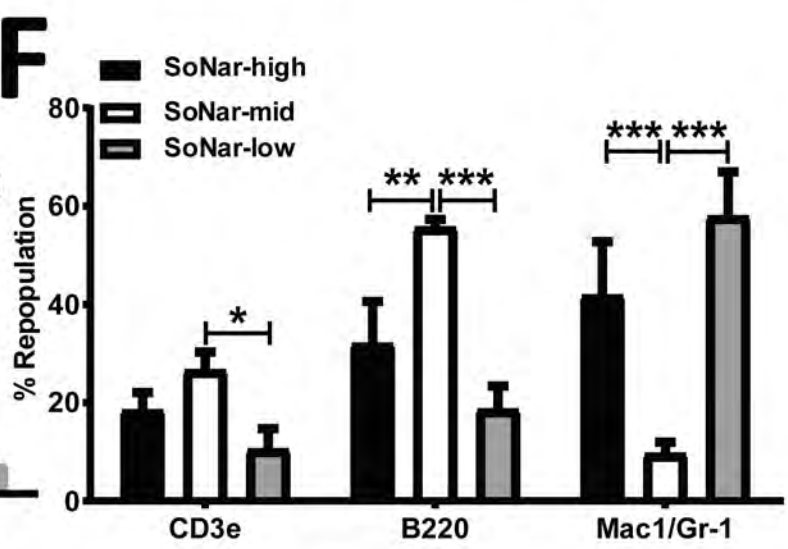

A
High:10.40%
Ratio:1.34
Mid:32.31%
Ratio:0.91
Low:10.23%
Ratio:0.56
Ex405
Ex488
7.50
0.22
30.60
4.25
1.74
30.52
3.62
0.20
38.11
SSC-A
Lin/CD48
c-Kit
Sca-1
c-Kit
CD150

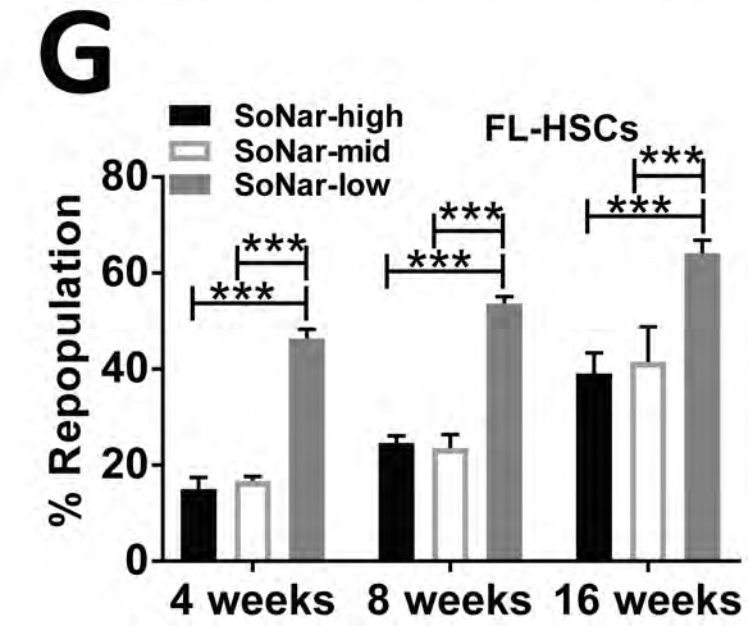

B
HSC frequency (%)
0.025
0.020
0.015
0.010
0.005
0.000
**
**
SoNar-high
SoNar-mid
SoNar-low


D
SoNar-high
SoNar-mid
SoNar-low
% Lineage
100
80
60
40
20
0
CD3e
B220
Mac-1/Gr-1
Ter119


C
1.03
30.40
c-Kit
Sca-1
c-Kit
CD150
Ex405
Ex488
Ex 405: 1764
Ex 488: 1917
Ratio: 0.92
MFI
2500
2000
1500
1000
500
0
Ex405
Ex488


E
SoNar-high
SoNar-mid
SoNar-low
% Repopulation
80
60
40
20
0
4 weeks
8 weeks
16 weeks


F
SoNar-high
SoNar-mid
SoNar-low
% Repopulation
80
60
40
20
0
CD3e
B220
Mac1/Gr-1


G
SoNar-high
SoNar-mid
SoNar-low
FL-HSCs
% Repopulation
80
60
40
20
0
4 weeks
8 weeks
16 weeks

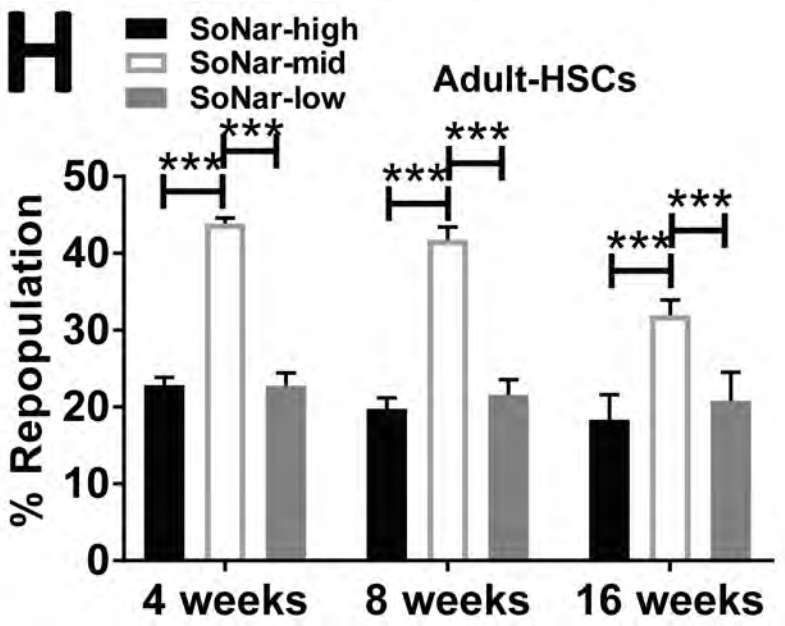
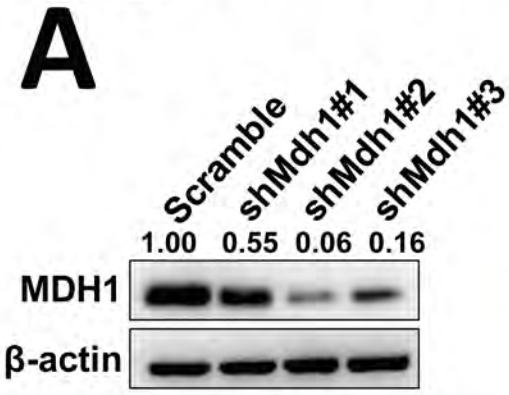
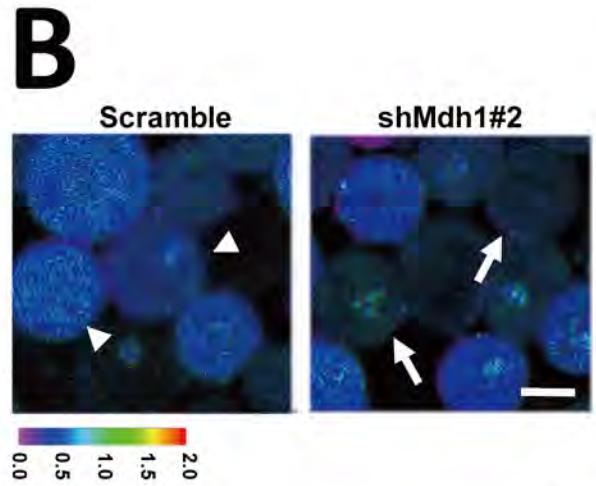
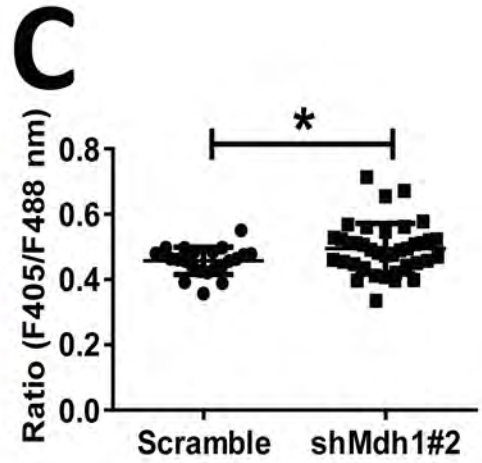

H
SoNar-high
SoNar-mid
SoNar-low
Adult-HSCs
% Repopulation
50
40
30
20
10
0
4 weeks
8 weeks
16 weeks

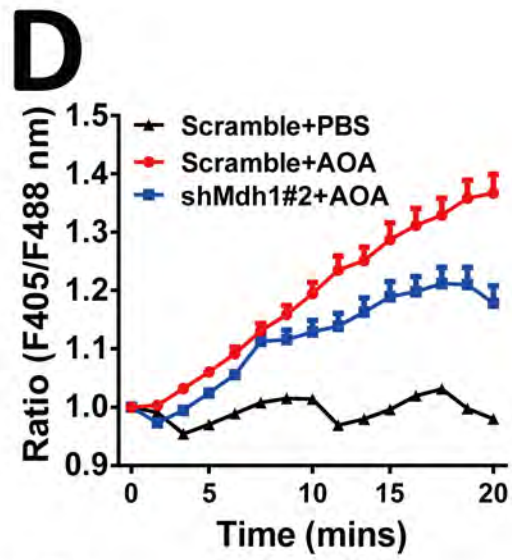
Figure S5, related to Figure 5. (**A** and **B**) Representative flow cytometric analyses of immunophenotypic $Lin^-Sca\text{-}1^+c\text{-}Kit^+CD150^+CD48^-$ LT-HSCs in SoNar-high, -mid and -low BM hematopoietic cell populations according to the ratios of SoNar fluorescence (A). Quantification of frequencies of LT-HSCs is shown (B, n=3). (**C**) Immunophenotypic $Lin^-Sca\text{-}1^+c\text{-}Kit^+CD150^+CD48^-$ adult-HSCs were gated and subjected for the analysis of the ratios of SoNar fluorescence. The mean fluorescence intensity (MFI) at excitation of 405 and 488 were quantified (n=5). (**D**) Frequencies of different lineages, including T cells ($CD3e^+$), B cells ($B220^+$), myeloid cells ($Mac\text{-}1^+Gr\text{-}1^+$), and erythroid cells ($Ter119^+$), were evaluated in $CD45^+$ SoNar-high, -mid and -low BM hematopoietic cells (n=8). (**E**) $CD45^+$ SoNar-high, -mid or -low BM cells along with CD45.1 competitor cells were transplanted into mice, followed by the analysis of the repopulation at 4, 8 and 16 weeks post-transplant (n=3 for SoNar-high group, n=7 for SoNar-mid group, n=3 for SoNar-low group). (**F**) Multilineage contribution of donor cells in the recipients at 16 weeks post-transplant (n=3 for SoNar-high group, n=7 for SoNar-mid group, n=3 for SoNar-low group). (**G** and **H**) The repopulated donor cells were analyzed in recipients transplanted with SoNar-high, -mid and -low FL-HSCs (G) or adult-HSCs (H) at 4, 8 and 16 weeks after transplantation (n=5). Data are represented as mean ± SEM. One-way ANOVA with Tukey's multiple comparison test (B), and two-way ANOVA with Sidak's multiple comparison test were used for the comparison of statistical significance (D-H). *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$.

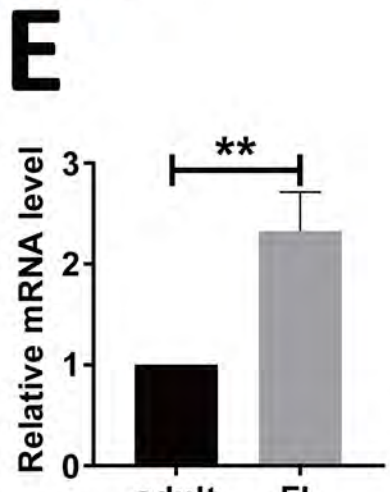
Figure S6

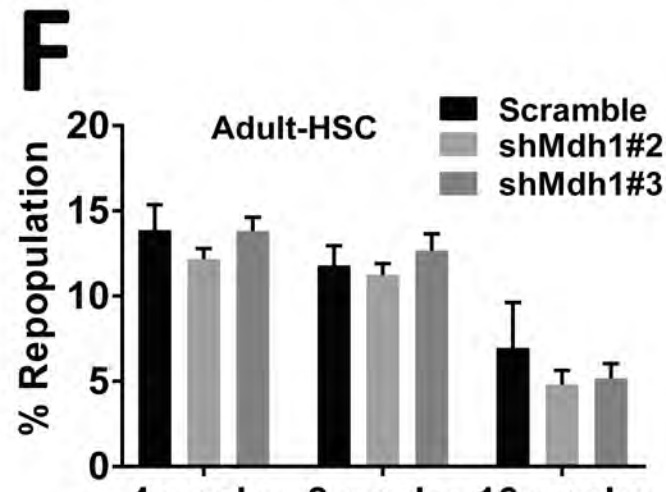

A
Scramble
shMdh1#1
shMdh1#2
shMdh1#3
1.00 0.55 0.06 0.16
MDH1
β-actin

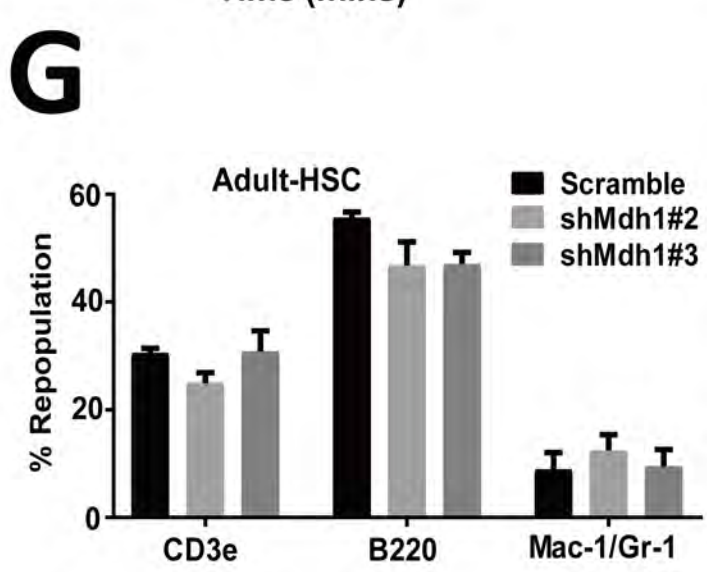

B
Scramble
shMdh1#2
0.0 0.5 1.0 1.5 2.0

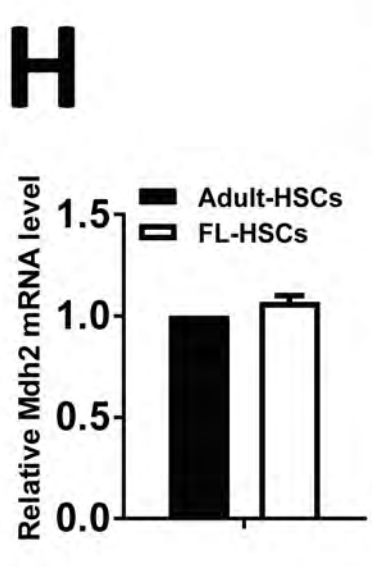

C
*
Ratio (F405/F488 nm)
0.0 0.2 0.4 0.6 0.8
Scramble
shMdh1#2

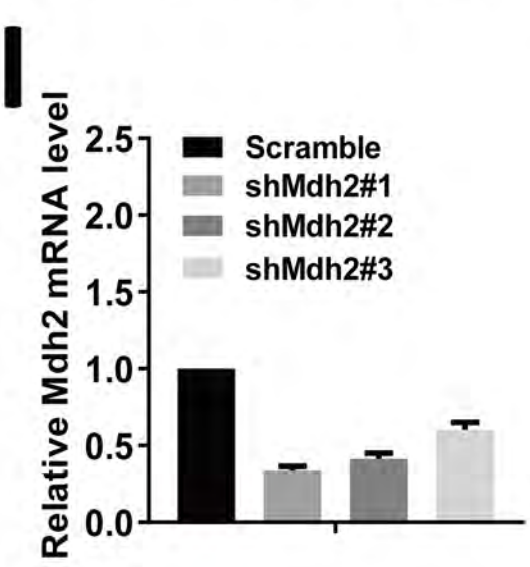

D
Ratio (F405/F488 nm)
Scramble+PBS
Scramble+AOA
shMdh1#2+AOA
0.9 1.0 1.1 1.2 1.3 1.4 1.5
0 5 10 15 20
Time (mins)

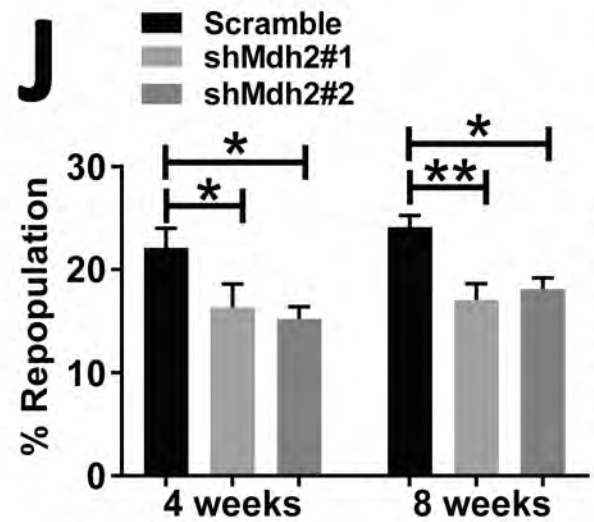

E
**
Relative mRNA level
0 1 2 3
adult
FL

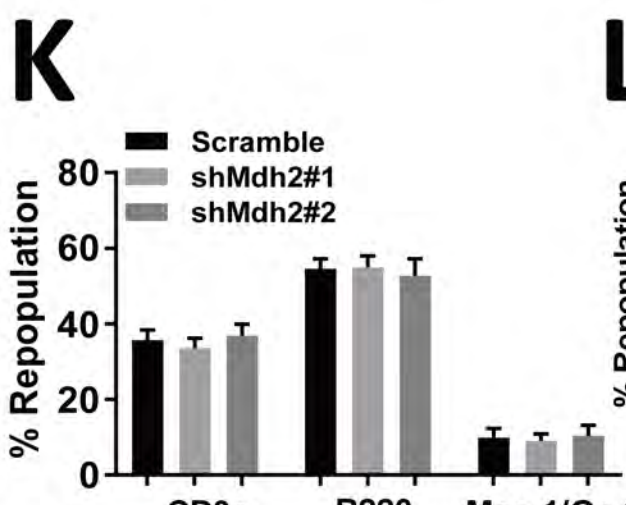

F
Adult-HSC
Scramble
shMdh1#2
shMdh1#3
% Repopulation
0 5 10 15 20
4 weeks
8 weeks
16 weeks


G
Adult-HSC
Scramble
shMdh1#2
shMdh1#3
% Repopulation
0 20 40 60
CD3e
B220
Mac-1/Gr-1


H
Adult-HSCs
FL-HSCs
Relative Mdh2 mRNA level
0.0 0.5 1.0 1.5


I
Scramble
shMdh2#1
shMdh2#2
shMdh2#3
Relative Mdh2 mRNA level
0.0 0.5 1.0 1.5 2.0 2.5


J
Scramble
shMdh2#1
shMdh2#2
% Repopulation
0 10 20 30
4 weeks
8 weeks


K
Scramble
shMdh2#1
shMdh2#2
% Repopulation
0 20 40 60 80
CD3e
B220
Mac-1/Gr-1

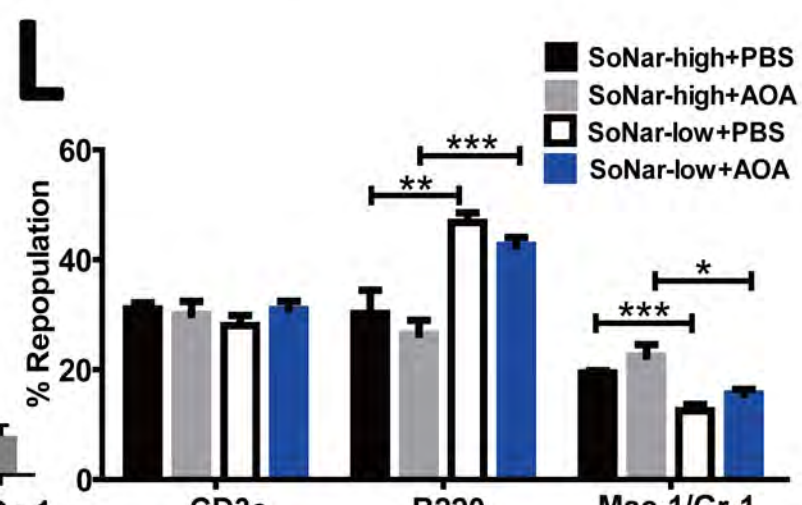

L
SoNar-high+PBS
SoNar-high+AOA
SoNar-low+PBS
SoNar-low+AOA
% Repopulation
0 20 40 60
CD3e
B220
Mac-1/Gr-1

Figure S6, related to Figure 6. (**A**) Knockdown efficiency of shRNAs targeting *Mdh1* (shMdh1#1-#3) was determined in 32D cells by immunoblotting. (**B**) Representative images for the ratios of SoNar fluorescence of *Mdh1*-knockdown and scrambled SoNar FL-HSCs. Arrowheads or arrows indicate SoNar-low and -high cells, respectively. Scale bar: 10 μm. (**C**) Quantification of the ratios of SoNar in panel B. A total of 25-40 SoNar FL-HSCs were analyzed. (**D**) Quantification of the ratios of SoNar fluorescence in SoNar FL-HSCs at indicated time points upon AOA incubation. A total of 25-40 SoNar FL-HSCs cells were analyzed. (**E-F**) *Mdh1* was silenced in $CD45^+$ BM hematopoietic cells by shRNA targeting *Mdh1* (shMdh1#2 or shMdh1#3) followed by transplantation into recipients. The repopulation was analyzed at 4, 8 and 16 weeks post-transplant (n=5). (**G**) Multilineage contribution of donor cells in the recipients at 16 weeks post-transplant (n=5). (**H**) Relative mRNA levels of *Mdh2* in FL-HSCs or adult-HSCs as determined by quantitative RT-PCR (n=3). (**I**) Knockdown efficiencies of shRNAs targeting to *Mdh2* (shMdh2#1-#3) were determined in L1210 cells by qRT-PCR (n=3). (**J-K**) *Mdh2* was silenced in $CD45^+$ BM hematopoietic cells by shRNA targeting *Mdh2* (shMdh2#1 or shMdh2#2) followed by transplantation into recipients. The repopulation was analyzed at 4 and 8 weeks post-transplant (J, n=5). Multilineage contribution of donor cells in the recipients at 8 weeks post-transplant in panel J are shown (K, n=5). (**L**) Multilineage contribution of donor cells in the recipients receiving SoNar-high and -low FL hematopoietic cells with AOA treatment at 16 weeks post-transplant (n=5). Data are represented as mean ± SEM. Student's two-tailed unpaired t test (C and E) or two-way ANOVA with Sidak's multiple comparison test (F, G, J, K and L) was

used for the comparison of statistical significance. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$.

Figure S7

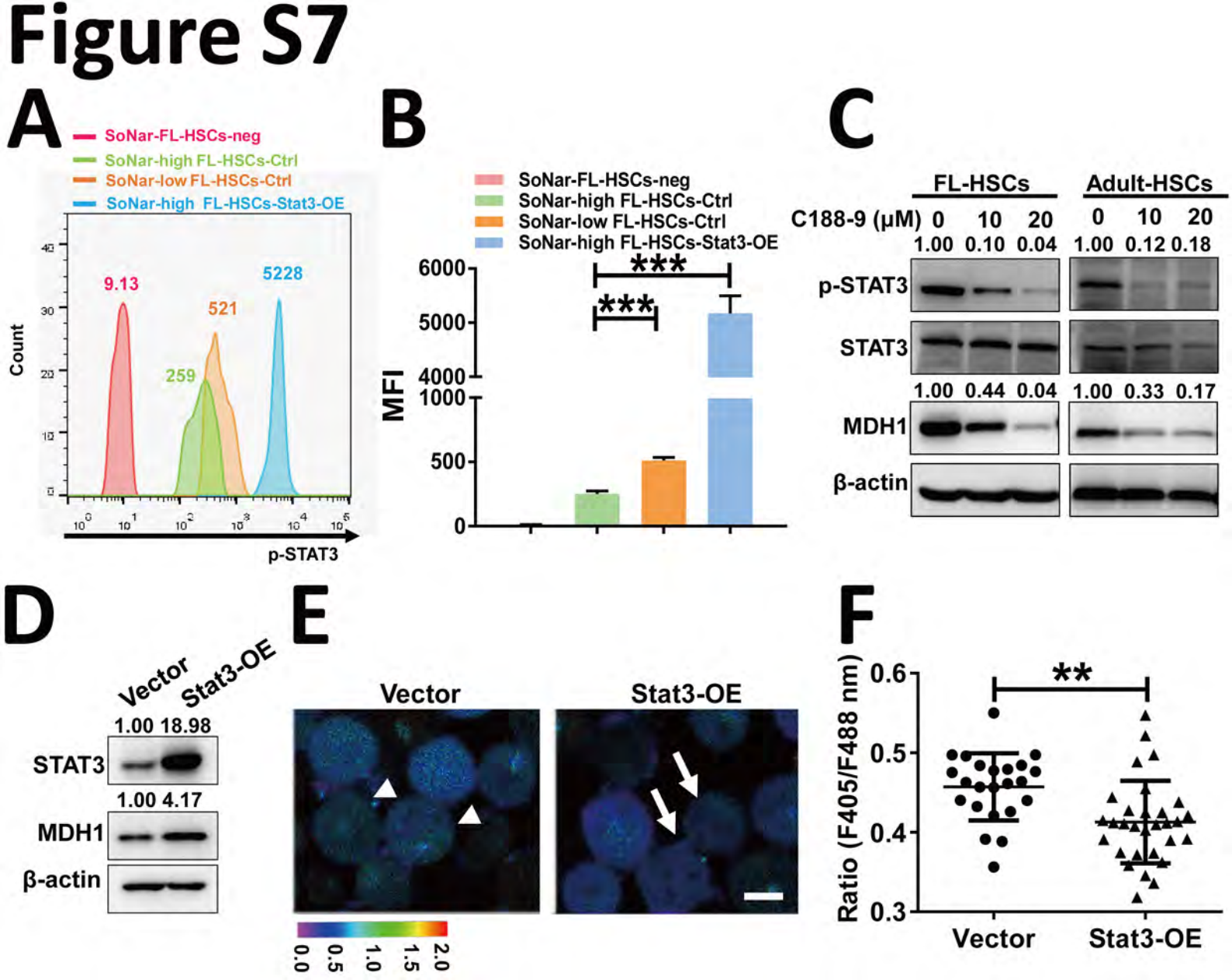

A
SoNar-FL-HSCs-neg
SoNar-high FL-HSCs-Ctrl
SoNar-low FL-HSCs-Ctrl
SoNar-high FL-HSCs-Stat3-OE
9.13
259
521
5228
Count
p-STAT3
B
SoNar-FL-HSCs-neg
SoNar-high FL-HSCs-Ctrl
SoNar-low FL-HSCs-Ctrl
SoNar-high FL-HSCs-Stat3-OE
***
***
MFI
6000
5000
4000
1000
500
0
C
FL-HSCs
Adult-HSCs
C188-9 (μM) 0 10 20 0 10 20
1.00 0.10 0.04 1.00 0.12 0.18
p-STAT3
STAT3
1.00 0.44 0.04 1.00 0.33 0.17
MDH1
β-actin
D
Vector
Stat3-OE
1.00 18.98
STAT3
1.00 4.17
MDH1
β-actin
E
Vector
Stat3-OE
0.0
0.5
1.0
1.5
2.0
F
**
Ratio (F405/F488 nm)
0.6
0.5
0.4
0.3
Vector
Stat3-OE

Figure S7, related to Figure 7. (**A**) Representative flow cytometric analysis of intracellular level of p-STAT3 of *Stat3*-overexpression SoNar-high FL-HSCs as compared to SoNar-low FL-HSCs. Ctrl, overexpression with control vector; neg, negative control. (**B**) Quantification data of mean fluorescence intensity (MFI) are shown (n=3). (**C**) The p-STAT3 and MDH1 level was examined in FL-HSCs or adult-HSCs after STAT3 inhibitor treatment with indicated doses by immunoblotting. Ratio of p-STAT3/STAT3, or MDH1/actin was quantified and normalized against untreated cells. (D) Protein level of MDH1 was measured in *Stat3*-overexpressed SoNar FL-HSCs and control cells by immunoblotting. Ratio of STAT3/actin, or MDH1/actin was quantified and normalized against control cells (vector). (**E**) *Stat3*-overexpressed SoNar FL-HSCs (*Stat3*-OE) and control cells (vector) were evaluated for the ratios of SoNar fluorescence and representative images are shown. Arrowheads or arrows indicate SoNar-high and -low cells, respectively. Scale bar: 10 μm. (**F**) Quantification of the ratios of SoNar fluorescence in panel E. A total of 25-30 SoNar FL-HSCs were analyzed. Data are represented as mean ± SEM. Student's two-tailed unpaired t test (F) or one-way ANOVA with Tukey's multiple comparison test (B) was used for the comparison of statistical significance. **, $p<0.01$; ***, $p<0.001$.