

Supplemental Table S1, List of antibodies.

Mouse anti- β -ACTIN	Sigma-Aldrich	Cat# A5316
Rabbit anti-NRF2	Abcam	Cat# Ab62352
Rabbit anti-NRF2	Santa Cruz Biotechnology	Cat# SC-13032x
Rabbit anti-GCLC	Abcam	Cat# Ab41463
Rabbit anti-NQO1	Abcam	Cat# Ab80588
Rabbit anti-HMOX1	Abcam	Cat# Ab68477
Rabbit anti-NQO1	Abcam	Cat# Ab80588
Rabbit anti-Catalase	Santa Cruz Biotechnology	Cat# SC-50508
Rabbit anti-GCLC	Abcam	Cat# Ab41463
Rabbit anti-GCLM	Abclonal	Cat# A5314
Rabbit anti-SLC7A11	Cell Signaling Technology	Cat# 12691
Rabbit anti-EZH2	Sigma-Aldrich	Cat# 07-689
Mouse anti-adult hemoglobin (HbA)	Santa Cruz Biotechnology	Cat# SC-21757
Mouse anti-fetal hemoglobin (HbF)	Santa Cruz Biotechnology	Cat# SC-21756
Sheep IgG isotype FITC control antibody	MyBioSource	Cat# MBS524511
FITC conjugated mouse anti-HbF	BD biosciences	Cat# 552829
Donkey anti-Mouse IgG, secondary, HRP	Santa Cruz Biotechnology	Cat# SC-2096
Donkey anti-Rabbit IgG, secondary, HRP	Santa Cruz Biotechnology	Cat# SC-2077

Supplemental Table S2, List of DNA oligoes.

cDNA analysis	Forward primer	Reverse primer
β -ACTB (both human and mouse)	GACGAGGCCCCAGAGCAAGAGAG G	TCTCAAACATGATCTGGGTCATC
CAT (both human and mouse)	GGTTTGGCCTCACAAGGACTACC	CGGTAGGGACAGTTCACAGGTAT
GCLC (both human and mouse)	GAGTATGGGAGTTACATGAT	TCTGGAAAGAAGAGGGGACTT
NQO1 (both human and mouse)	ATCCTGGAAGGATGGAAGAAAC	TCTAGCTTTGATCTGGTTGTCAG
GCLM (both human and mouse)	AAGTGCCCGTCCACGCACAG	CTTCTAGTTGATGATGAAGA
SLC7A11 (both human and mouse)	CTCCAGAACACGGGCAGCGT	CAAATGCCAGGGATATCACA
KDM6a (human)	TCACTTCAACCTCTTATTGGAAG	CTTTGAACATAAGCCCAAGTCGT
KDM6b (human)	TCCTCCTGCCACCAAAATACCTC	CCAGCCCATCAGGTAGGATCTTG
EZH1 (human)	TGGTTCCCATCATGTATTCCTGG	GATCCAGGGATCATCTCTTCTTC
EZH2 (human)	ATGGGCCAGACTGGGAAGAAAT C	GCGCAATGAGCTCACAGAAGTCA
HBG1 (human)	GTGGATCCTGAGAACTTCA	GCTTGCAGAATAAAGCCTATCCTTG
HBA (human)	GTGGATCCTGAGAACTTCA	TTAGGCAGAATCCAGATGCTCAAGG
Tgfb (mouse)	GGTGCTCGCTTTGTACAACA	ACTGCTTCCCGAATGTCTGA
Tgfa (mouse)	CATTGAGCCCACCCTTGTTT	ATGAGGAACAGGCAGCTTCT
Il1b (mouse)	ACTCATTGTGGCTGTGGAGA	TGTTGTTTCTCTCGGAGCCT
Il6 (mouse)	CTGGGGATGTCTGTAGCTCA	CAGGTCTGTTGGGAGTGGTA

<i>Ccl2</i> (mouse)	AGGTGTCCCAAAGAAGCTGT	ACAGAAGTGCTTGAGGTGGT
<i>Ccl3</i> (mouse)	GATCTGCGCTGACTCCAAAG	GTCCCTCGATGTGGCTACTT
<i>Ccl4</i> (mouse)	CCTCTCTCTCCTCTTGCTCG	CTCTCCTGAAGTGGCTCCTC
<i>Ccl5</i> (mouse)	TGCCCACGTCAAGGAGTATT	AGATGCCCATTTTCCCAGGA
<i>Ccl7</i> (mouse)	TGAAGCCAGCTCTCTCACTC	TATAGCCTCCTCGACCCACT
<i>Ccl11</i> (mouse)	CACAAAGCACCTGGACCAAA	TCGTCCCATTGTGTTCTCTCA
<i>Ccl17</i> (mouse)	GCTTCTGGGGACTTTTCTGC	TTGAAACCATGGACAGCAGC
<i>Cxcl1</i> (mouse)	AGTTCCAGCACTCCAGACTC	CTCGCGACCATTCTTGAGTG
<i>Cxcl10</i> (mouse)	ACATCAGCTGCTACTCCTCC	CTGAGCTAGGGAGGACAAGG
ChIP analysis	Forward primer	Reverse primer
<i>HBG1</i> (human)	CTGAAACGGTCCCTGGCTA	CTGTGAAATGACCCATGGCG
<i>HBA</i> (human)	CACTTAGACCTCACCTGTGGAG CCACACCCTAGGGTTGGC	CTTGTAACCTTGATACCAACCTG
<i>HMOX1</i> ARE (human)	CACGGTCCCGAGGTCTATT	AAGGGTGGAGGAGCTGCTAT
<i>NQO1</i> ARE (human)	ATTACCTGCCTTGAGGAGCA	CAGAGGCCTCAAAAATCTGG
<i>SLC7A11</i> ARE (human)	TGCATGAGGAAAATGATCCA	GCATGGAAAAGGTCAGAACC
<i>Nqo1</i> ARE (mouse)	TTTCTAAGAGCAGAACGCAGCAC	AGACCTCCTGGGTACAAAATGGA
<i>Cat</i> ARE (mouse)	GTAGGGAGAGACACGGTTTCCA	AGAAAAGACAAATCAAGAACCAG
<i>Hmox1</i> ARE (mouse)	AGTCACGGTCCCGAGGTCT	TCGAGTTGATCTTCTTACAGTG
<i>Gclc</i> ARE (mouse)	CTCTTAACCGCTGAGCCATC	TATTGGGAGATGGGGAGAGA
<i>Slc7a11</i> ARE (mouse)	AAATTTCCGGCTTTGAGCTA	CTTGTCAGCACAGCGTGATT
shRNA constructs	Forward primer	Reverse primer
shControl	CCGGCCTAAGGTTAAGTCGCCCT CGCTCGAGCGAGGGCGACTTAA CCTTAGGTTTTTG	AATTCAAAAACCTAAGGTTAAGTCGC CCTCGCTCGAGCGAGGGCGACTTAA CCTTAGG
shEZH2 construct 1	CCGGTGACTTCTGTGAGCTCATT GCCTCGAGGCAATGAGCTCACA GAAGTCATTTTTG	AATTCAAAAATGACTTCTGTGAGCTC ATTGCCTCGAGGCAATGAGCTCACA GAAGTCA
shEZH2 construct 2	CCGGGTTTGTGGCGGAAGCGT GTACTCGAGTACACGCTTCCGCC AACAACTTTTTG	AATTCAAAAAGTTTGTGGCGGAAGC GTGTACTCGAGTACACGCTTCCGCC AACAAAC

Supplemental Figures

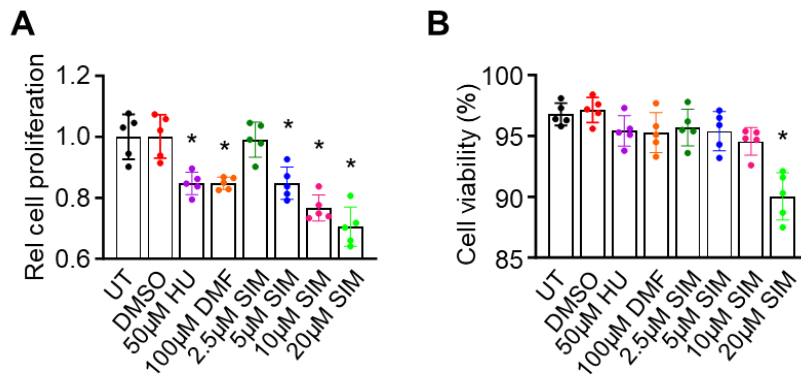


Figure S1, Effect of HbF inducers on cellular proliferation and viability of SCD erythroblasts. Cellular proliferation (A) and viability (B) of SCD erythroblasts at day 12 after 48 h of treatments with 0.1% DMSO, 50 μ M hydroxyurea (HU), 100 μ M dimethyl fumarate (DMF), 2.5-20 μ M simvastatin (SIM), or untreated control (UT). Data represents mean $\pm$ SD of three biological replicates. *, $p < 0.05$.

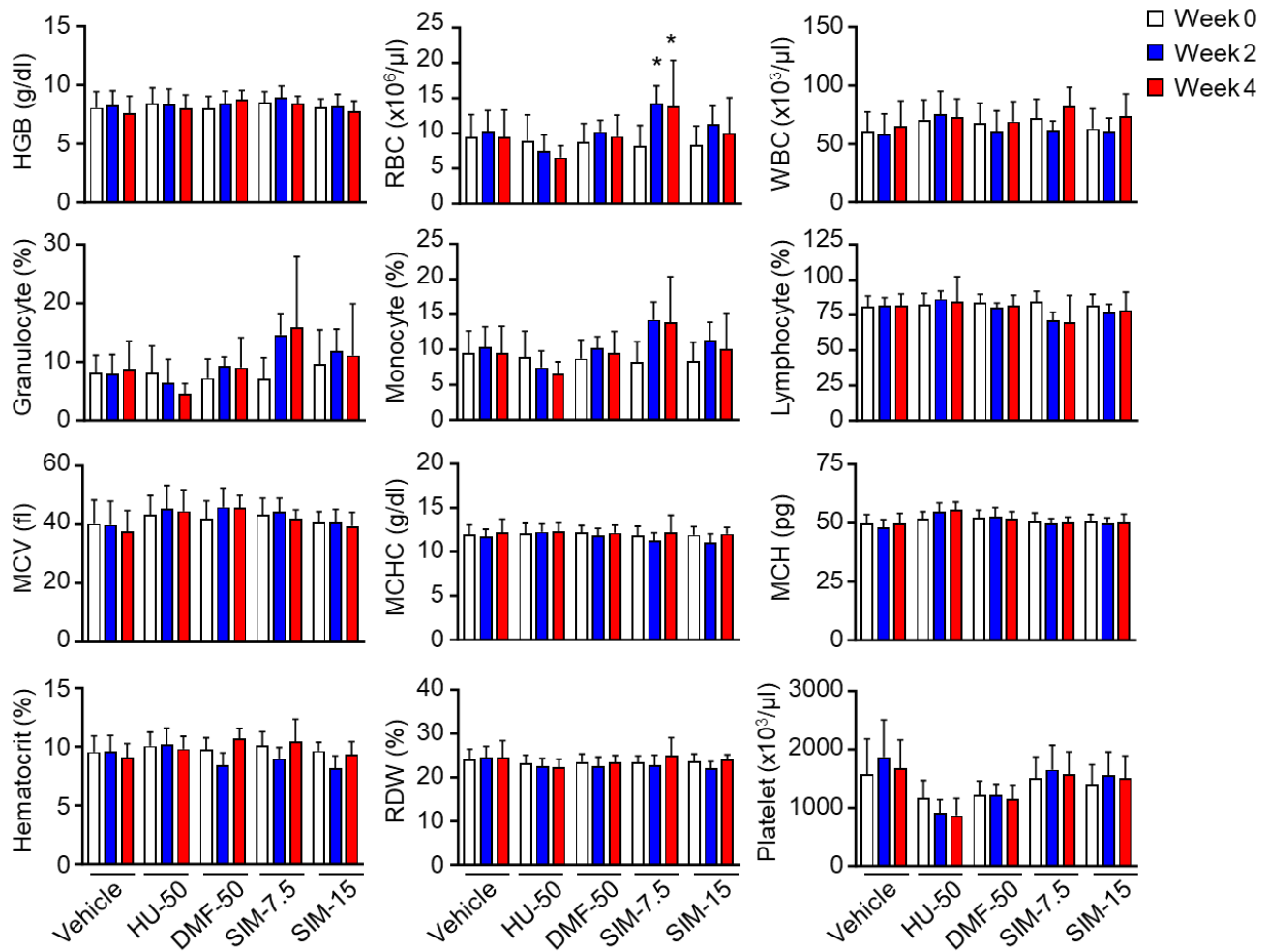


Figure S2, Hematological indices of SCD mice treated with simvastatin. Complete blood count and differentials for peripheral blood of the SCD mice, at week 0, week 2, and week 4 of treatment of simvastatin (SIM, 7.5-15 mg/kg), hydroxyurea (HU, 50 mg/kg) or dimethyl fumarate (DMF, 50 mg/kg) daily, 5 days a week. One-way ANOVA with Bonferroni's multiple comparison test was used for statistical analysis (n=5 mice). *, $p < 0.05$.