**Figure S1. Emetine dissolves spontaneous and arsenite-induced SGs.**

Differentiating CD34+ cells were collected at different days of *in vitro* differentiation (Day 6 is shown here) and cultured in the absence (UN, upper panel) or presence (EM, upper panel) of emetine (20 μM) for 120 minutes before processing for immunofluorescence microscopy using antibodies specific for SGs (eIF3b, green), PBs (S6K1-hedls, red) or SGs/PBs (eIF4E, blue). Alternatively, cells were cultured in the absence (SA, lower panel) or presence (EM, lower panel) of emetine for 60 minutes before adding sodium arsenite (500 μM) for 45 minutes and processing for immunofluorescence microscopy. Enlarged views (3.2 fold) of boxed areas depict separate channels and merged views of SGs/PS with or without different drug treatments.

**Figure S2. CD34+ bone marrow cells lineage differentiation in *in vitro* culture. (A)** CD34+ cells, collected at different days of *in vitro* differentiation in media supporting erythroid, myeloid and megakaryocytic differentiation were stained with MGG to identify the morphology of the cells. Representative erythroid cells are shown (magnification 50x). **(B)** Differentiating CD34+ cells, cultured in the same conditions described in panel A, were also stained for cell surface markers specific for mature erythrocytes (GlyA-FITC), megakaryocytes (CD41-FITC) or myeloid cells (CD11b-PECy5) to assess lineage differentiation. **(C)** Percentage of hemoglobin-positive CD34+ cells, assed by DAF staining, is also shown. Data are the means ± SEM from three independent experiments. **(D)** Percentage of immature (CD71+/GlyA-) and mature (CD71+/GlyA+) erythroid cells containing SGs on the 6th day of *in vitro* differentiation. Values are the means of three independent experiments in which at least 100 cells were counted. **(E)** HRI knockdown efficiency in CD34+ hematopoietic cells was investigated using RT-qPCR and reported as mRNA level of the target gene normalized against β-actin housekeeping gene expression

level. Results represent the means of three independent experiments performed in triplicate ± SEM. P value shows t-test probability compared to FLuc treated samples.

**Figure S3. Mice blood parameters and SGs positive erythroid cells in whole murine and human bone marrow samples. (A)** Mice normal physiological parameters recorded at the time of sacrifice for bone marrow staining shown in Figure 2. Averages with standard deviation are shown for 7 mice. **(B)** The percentage of immature (CD71+/Ter119-) and mature (CD71+/Ter119+) murine erythroid cells containing SGs was calculated by immunofluorescence microscopy. Values are the means of three independent fields in which at least 100 cells were counted. **(C)** Percentage of immature (CD71+/GlyA-) and mature (CD71+/GlyA+) erythroid cells containing SGs, from a healthy human donor's whole bone marrow. Values are the means of three independent fields in which at least 100 cells were counted.

**Figure S4. HRI, G3BP and $\alpha$-globin mRNA levels and absolute numbers of cell viability. (A)** Efficiency of G3BP knockdown in CD34+ hematopoietic cells. G3BP efficiency was investigated using RT-qPCR and reported as mRNA level of the target gene normalized against $\beta$-actin housekeeping gene expression level. Results represent the means of three independent experiments performed in triplicate ± SEM. P value shows t-test probability compared to FLuc treated samples. **(B)** Real-time PCR was used to quantify $\alpha$-globin mRNA level. mRNA expression levels are normalized against $\beta$-actin housekeeping transcripts. Results represent the means of three independent experiments performed in triplicate ± SEM. P values are derived from student's t-test compared to FLuc infected samples. **(C)** Absolute numbers of live and dead cells after 7 days **(A)** of G3BP knock down treatment.

*May-Grünwald-Giemsa staining and DAF*

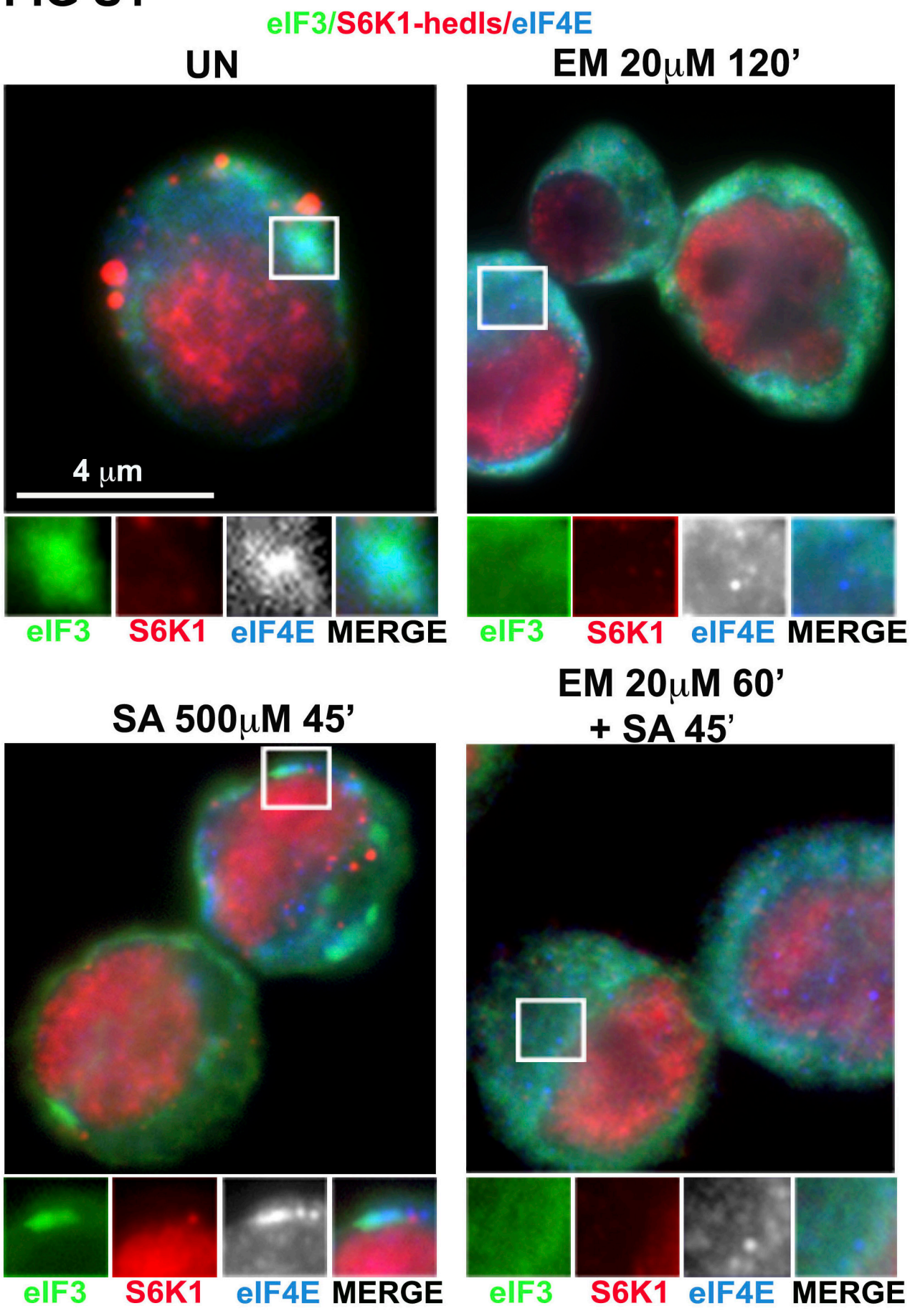
At least $10X10^5$ CD 34+ cells were collected at different days of the *in vitro* differentiation and were cytospun on the slides and air dried. Slides were then placed in methanol for 5 minutes, air dried and placed in MGG (Sigma-Aldrich) stain for 10 min. Slides were then rinsed with water and allowed to air dry before examination with immersion oil and 50X objective.

Hemoglobinization of *in vitro* differentiating human CD34+ was assayed by DAF (2,7-diaminofluorene; Sigma-Aldrich) staining at different days of culture. Assay was performed as previously described [24], with minor modifications. At least 300 cells per sample were scored and blue cells were counted positive.

*Quantitative real-time PCR*

RT-qPCR on CD34+ cells was performed as follows: 200 ng of total RNA from CD34+ cells infected with Lentiviruses containing shRNA against Firefly luciferase or HRI or G3BP was used to generate first strand cDNA using oligo dT primers from the Superscript III reverse transcription kit (Invitrogen). RT–qPCR was performed using Taqman supermix (Applied Biosystems) for HRI and SYBRgreen supermix (Applied Biosystems) for G3BP in a 7900HT Sequence Detection System (Applied Biosystems). Beta actin was used as an internal control. Relative changes of mRNA amounts were calculated based on the ΔΔCt method. HRI Taqman Expression System (Hs 00205264_m1) and Taqman β-actin probe (401846) were purchased from Applied Biosystems. Primers for G3BP (Forward, CTTATGTCCATGGGGGATTG; Reverse, TCACCTGGACTACCACACCA), and α-globin (Forward, ACTGAACCTGACCGTACAACGCTGGCGAGT; Reverse, AGCAGGCAGTGGCTTAGAG) were purchased from IDT, Integrated DNA Technologies Inc., Coralville, IA, USA.

# FIG S1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4 μm
eIF3
S6K1
eIF4E
MERGE
eIF3
S6K1
eIF4E
MERGE
SA 500μM 45'
EM 20μM 60'
+ SA 45'
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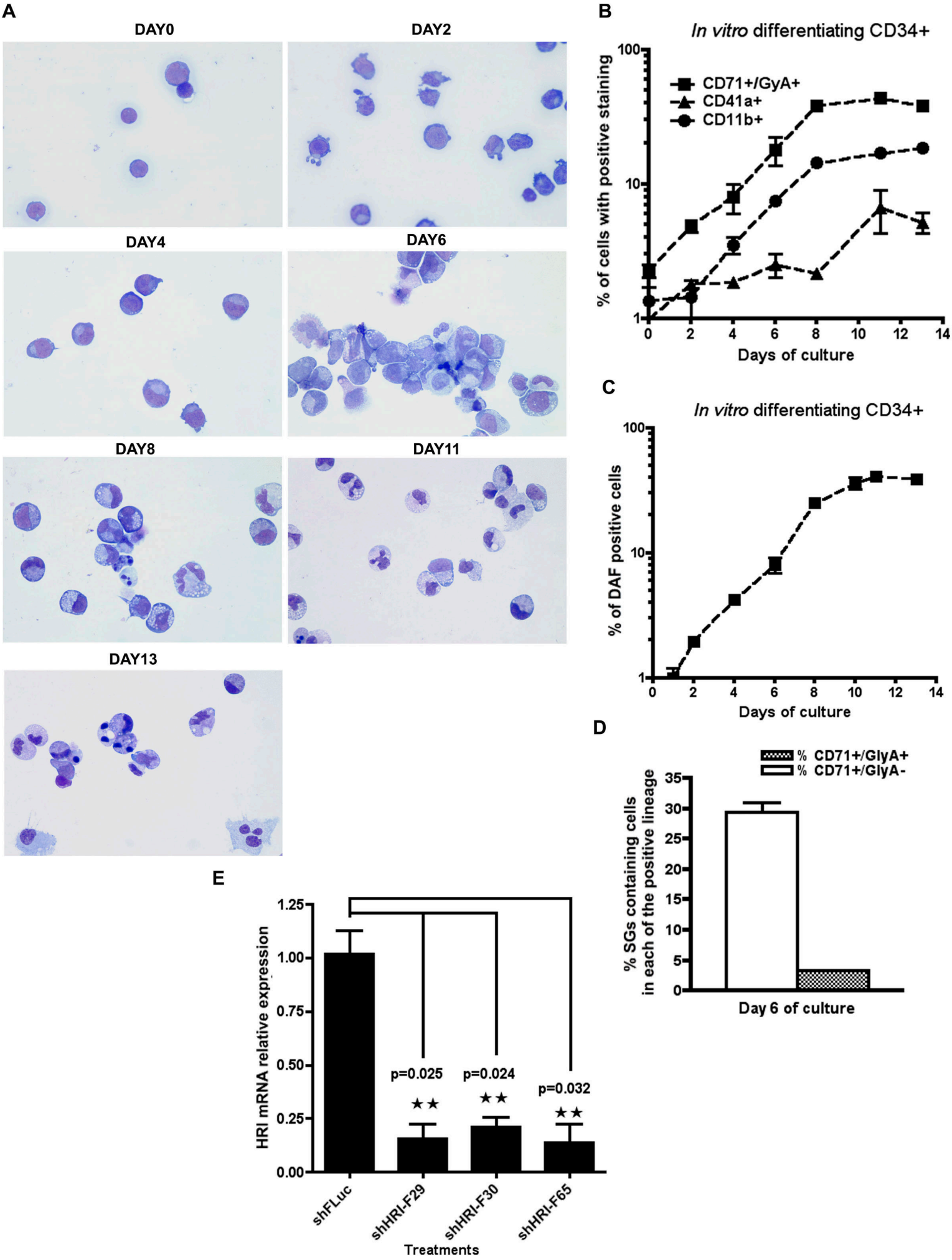
S6K1
eIF4E
MERGE
eIF3
S6K1
eIF4E
MERGE

FIG S2

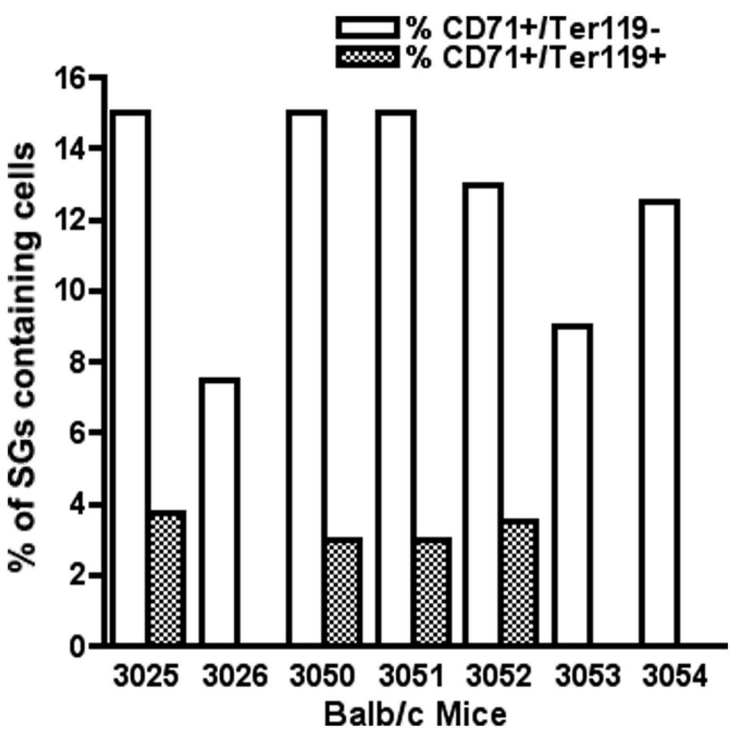

A
DAY0
DAY2
DAY4
DAY6
DAY8
DAY11
DAY13
B
In vitro differentiating CD34+
% of cells with positive staining
CD71+/GyA+
CD41a+
CD11b+
Days of culture
C
In vitro differentiating CD34+
% of DAF positive cells
Days of culture
D
% CD71+/GlyA+
% CD71+/GlyA-
% SGs containing cells in each of the positive lineage
Day 6 of culture
E
HRI mRNA relative expression
p=0.025
p=0.024
p=0.032
shFLuc
shHRI-F29
shHRI-F30
shHRI-F65
Treatments

# FIG S3

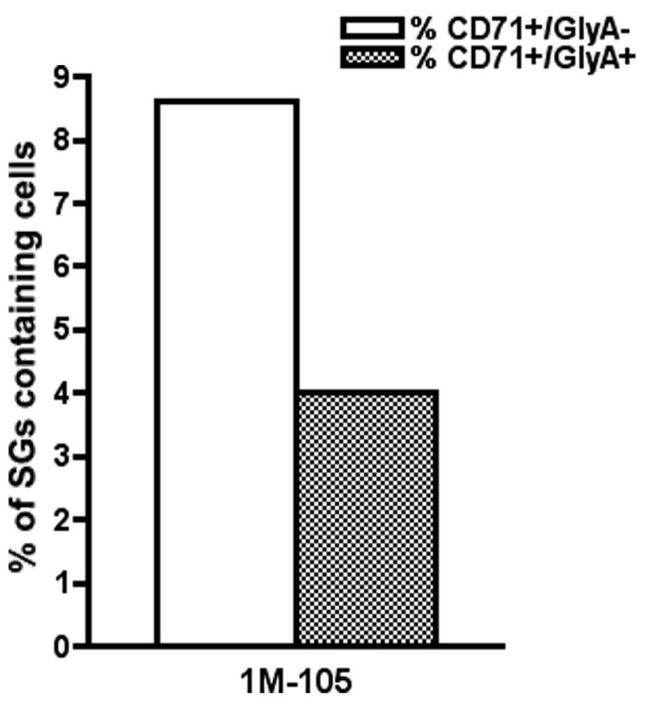
A

| Normal Hematological Parameters | |
|---|---|
| Number of Mice | 7 |
| White blood counts (k/ul) | 5.4971 +/- 1.9600 |
| HCT (%) | 54.3286 +/- 2.2199 |
| Platelet counts (k/ul) | 583.0000 +/- 350.0100 |

B

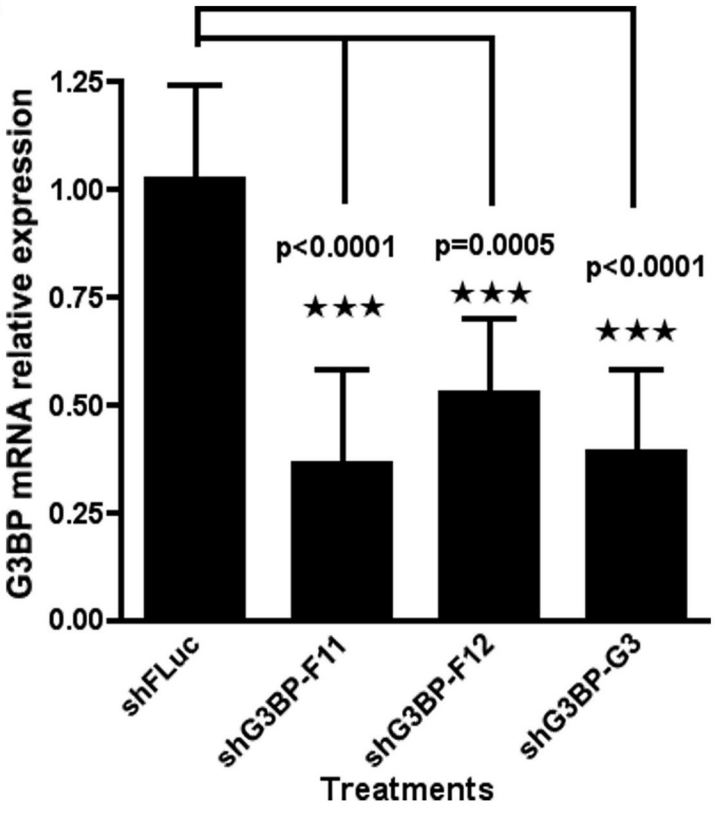



C

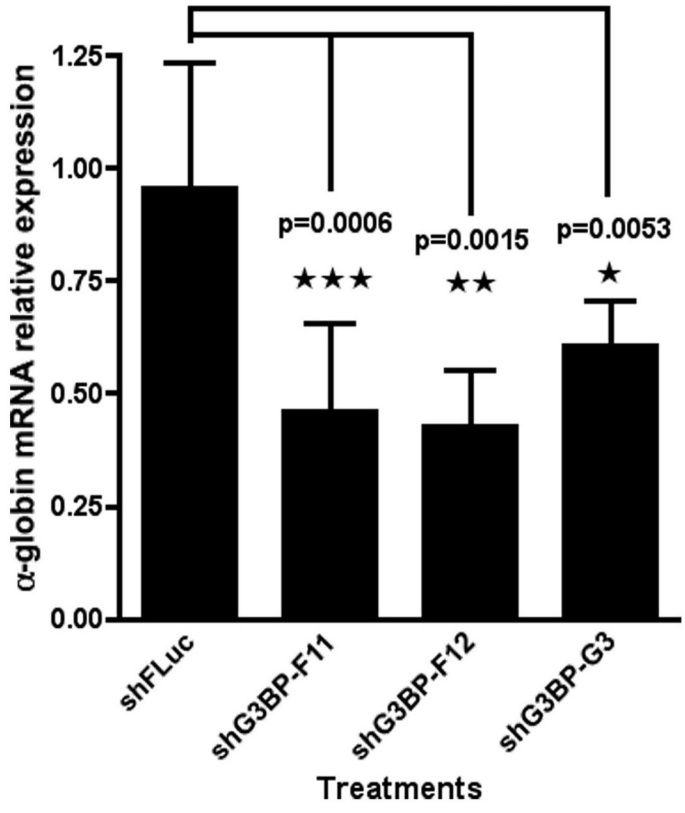


# FIG S4

A




B




C

| Treatments (DAY 7) | Absolute number of live cells (x10E4) | Absolute number of dead cells (x10E4) |
|---|---|---|
| shFLuc | 172 +/- 2.08 | 12 +/- 2.89 |
| shG3BP-G3 | 113 +/- 1.53 | 37 +/- 1.15 |
| shG3BP-F11 | 164 +/- 0.58 | 32 +/- 2.08 |
| shG3BP-F12 | 145 +/- 2.64 | 35 +/- 4.58 |

**Supplementary Information Table S1.** List of antibodies and siRNA/shRNA target sequences used in this study.

| **Antibody** | **Source** |
|---|---|
| Goat anti-eIF3b | Santa Cruz Biotechnology |
| Goat anti-TIA-1 | Santa Cruz Biotechnology |
| Mouse anti-S6K1 | Santa Cruz Biotechnology |
| Rabbit anti-eIF4E | Santa Cruz Biotechnology |
| Rabbit anti-eIF4G | Santa Cruz Biotechnology |
| Rabbit anti-RCK | Bethyl Laboratories |
| Mouse anti-G3BP | BD Biosciences |
| Rabbit anti-G3BP | Bethyl Laboratories |
| Rabbit anti-eIF2$\alpha$ | Santa Cruz Biotechnology |
| Rabbit anti-Phospho S51-eIF2$\alpha$ | StressGen |
| Rabbit anti-$\alpha$globin 898 | Dr Weiss, Philadelphia |
| Rabbit anti-GAPDH | Santa Cruz Biotechnology |
| Anti-human CD71-PECy5-conjugated antibody | BD Biosciences |
| Anti-human GLYA-FITC-conjugated antibody | BD Biosciences |
| Anti-human CD11b-PECy5-conjugated antibody | BD Biosciences |
| Anti-human CD41a-FITC-conjugated antibody | BD Biosciences |
| Anti-mouse CD71-FITC-conjugated antibody | BD Pharmigen |
| Anti-mouse TER119-APC-conjugated antibody | BD Pharmigen |
| Anti-mouse CD41-FITC-conjugated antibody | BD Pharmigen |
| Anti-mouse CD11b-ALEXA FLUOR 488-conjugated antibody | BD Pharmigen |
| Cy2-HRP-conjugated secondary antibodies | Jackson Immunoresearch Labs |
| Cy3-HRP-conjugated secondary antibodies | Jackson Immunoresearch Labs |
| Cy5-HRP-conjugated secondary antibodies | Jackson Immunoresearch Labs |

| **shRNA Target sequence** | **Source** |
|---|---|
| *Firefly Luciferase* | The RNAi Consortium, Broad Institute |
| G3BP-G3 CCAGGCTTTGAGGAGATTCAT | The RNAi Consortium, Broad Institute |
| G3BP-F11 GCCTGTAAGAAATACAGGATT | The RNAi Consortium, Broad Institute |
| G3BP-F12 CGGGAATTTGTGAGACAGTAT | The RNAi Consortium, Broad Institute |

| **shRNA Target sequence** | **Source** |
|---|---|
| *Firefly Luciferase* | The RNAi Consortium, Broad Institute |
| HRI-29 GGATTGGATAGTCGAGAGAAA | The RNAi Consortium, Broad Institute |
| HRI-30 GAATTGGTAGAAGGTGTGTTT | The RNAi Consortium, Broad Institute |
| HRI-65 CAGAGCTATTACTCACTTAAT | The RNAi Consortium, Broad Institute |