LETTER TO THE EDITOR

IDH1-mutated B-cell acute lymphoblastic leukemia characterized by oncogenic reprogramming of lipid metabolism

Authors

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Supplementary information

Table S1. Univariate and multivariate analysis for EFS in B-ALL.

Parameter	EFS					
	Univariate			Multivariate		
	P	HR	95%CI	P	HR	95%CI
IDH1 (mutated vs. WT)	0.017	1.882	1.118-3.166	0.013	2.199	1.181-4.095
TP53 (mutated vs. WT)	0.127	1.604	0.874-2.942	0.166	1.582	0.827-3.027
NRAS (mutated vs. WT)	0.582	1.194	0.636-2.240	0.387	1.366	0.673-2.773
KRAS (mutated vs. WT)	0.285	1.456	0.732-2.896	0.143	1.781	0.822-3.858
Age (≥35 vs. <35 years)	0.164	1.353	0.884-2.070	0.418	1.220	0.754-1.975
Gender (male vs. female)	0.569	1.125	0.749-1.690	0.953	1.013	0.664-1.546
WBC (≥30 vs. <30 $\times 10^9$/L)	0.050	1.575	1.000-2.479	0.006	2.035	1.231-3.366
HB (≥100 vs. <100 g/L)	0.652	0.908	0.596-1.383	0.978	1.006	0.649-1.560
PLT (100 vs. <100 $\times 10^9$/L)	0.550	0.876	0.569-1.350	0.477	0.853	0.550-1.323

Supplementary Figure legend

Figure S1. LDs was induced by OA and R-2HG in B-ALL cell lines. A. After BALL-1 and RS4-11 were treated with OA (100μM) or DMSO for 24h, LDs were stained with Lipi-Blue dye. The bar graph represented the mean fluorescence intensity of cells stained with Lipi-Blue dye. B. The TG levels were measured in B-ALL cells with 24-hour treatment of OA (100μM) or DMSO. C. Wright-Giemsa staining of BALL-1 and RS4-11 cells treated with OA (100μM) or DMSO for 24h was captured at 400× magnifications. Red arrows indicate the locations of prominent lipid droplets. D. LDs were stained with Lipi-Blue dye in BALL-1 and RS4-11 cells treated with R-2HG (300μM) or DMSO for 24h. The bar graph represented the mean fluorescence intensity of cells stained with Lipi-Blue dye. E. TG measurement in B-ALL cells with 24-hour treatment of R-2HG (300μM) or DMSO. F. Wright-Giemsa staining of BALL-1 and RS4-11 cells treated with R-2HG (300μM) or DMSO for 24h was captured at 400× magnifications. Red arrows indicate the locations of prominent lipid droplets. G. Wright-Giemsa staining of $IDH1^{R132S}$-overexpressed BALL-1 and RS4-11 cells was captured at 400× magnifications. Red arrows indicate the locations of prominent lipid droplets. H. $IDH1^{R132S}$-overexpressed BALL-1 and RS4-11 cells were treated with AG120 (500nM) or DMSO for 24h, LDs were stained with Lipi-Blue dye. The bar graph represented the mean fluorescence intensity of cells stained with Lipi-Blue dye. Data are presented as mean ± SEM from three independent experiments (n=3). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.`

Figure S2. Impacts of R-2HG and *IDH1*^{R132S} mutation on the proliferation of B-ALL cell lines. A. B-ALL cell lines (BALL-1, REH and RS4-11) and AML cell line (MV4-11) were treated with different concentrations of R-2HG for 96h and cell viability was analyzed. B. Proliferation curve was draw for B-ALL cell lines and MV4-11 treated with R-2HG (300μM) or DMSO. C. Apoptotic analysis was conducted after B-ALL cell lines were treated with R-2HG (300μM) or DMSO for 96h. D. Western blot detected mutant IDH1 in *IDH1*^{R132S}-overexpressed B-ALL cell lines. E. Proliferation curve was draw for B-ALL cell lines transfected with *IDH1*^{R132S} mutants. F. Apoptosis was detected in *IDH1*^{R132S}-overexpressed B-ALL cell lines supplemented by 10% FBS for 72h. The representative FCM analysis of REH cells was shown. Data are presented as mean ± SEM from three independent experiments (n=3). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ns = no significance.

Figure S1

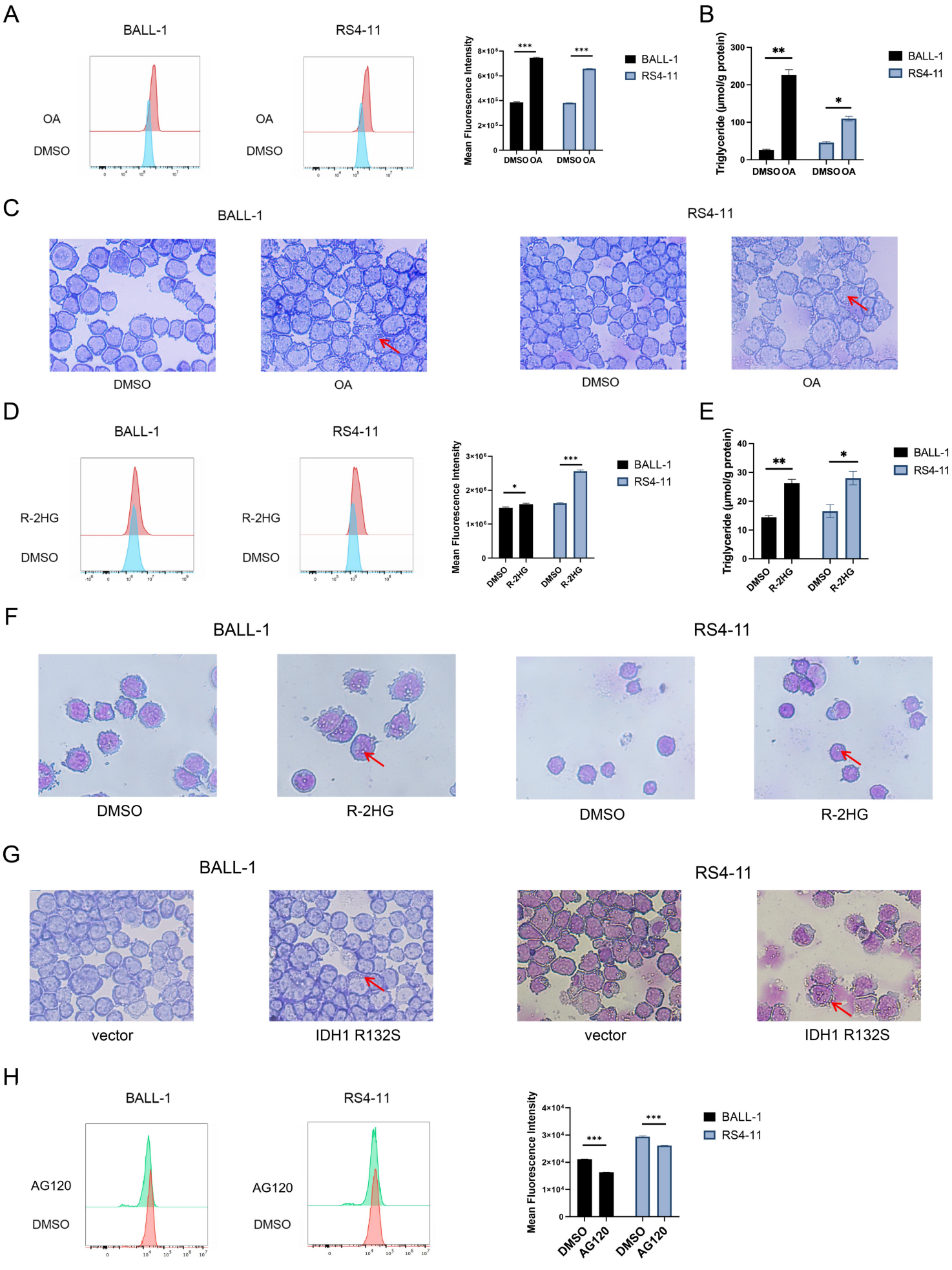
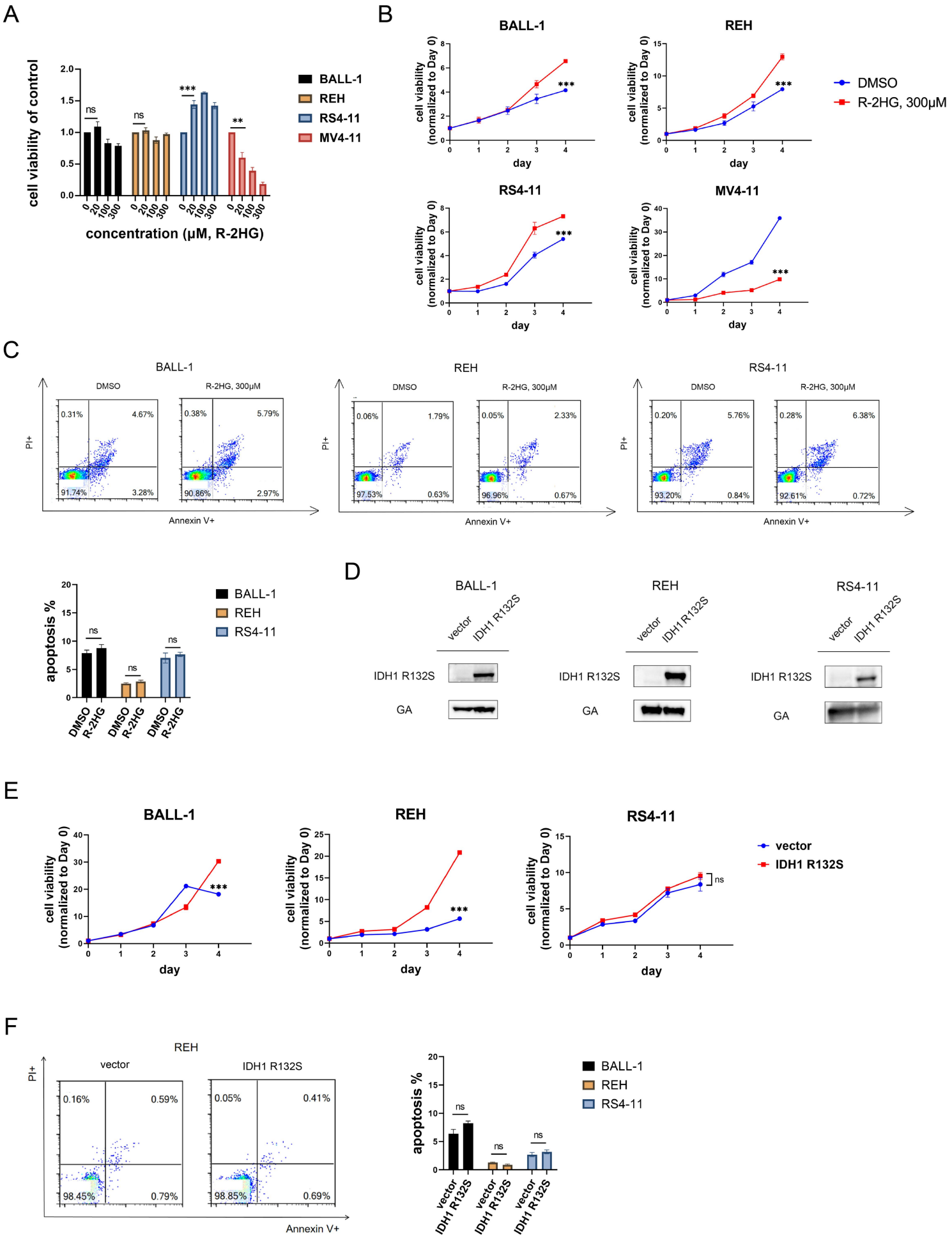

A
BALL-1
RS4-11
OA
DMSO
Mean Fluorescence Intensity
BALL-1
RS4-11
DMSO OA
B
Triglyceride (μmol/g protein)
C
BALL-1
RS4-11
DMSO
OA
D
R-2HG
E
F
G
vector
IDH1 R132S
H
AG120

Figure S2


A
cell viability of control
concentration (μM, R-2HG)
BALL-1
REH
RS4-11
MV4-11
B
BALL-1
REH
RS4-11
MV4-11
cell viability (normalized to Day 0)
day
DMSO
R-2HG, 300μM
C
BALL-1
REH
RS4-11
DMSO
R-2HG, 300μM
PI+
Annexin V+
0.31%
4.67%
91.74%
3.28%
0.38%
5.79%
90.86%
2.97%
0.06%
1.79%
97.53%
0.63%
0.05%
2.33%
96.96%
0.67%
0.20%
5.76%
93.20%
0.84%
0.28%
6.38%
92.61%
0.72%
apoptosis %
D
vector
IDH1 R132S
GA
E
F
REH
vector
IDH1 R132S
0.16%
0.59%
98.45%
0.79%
0.05%
0.41%
98.85%
0.69%