Figure S1. HL-60R cell viability is not affected by a large dose range of cytarabine. HL-60R cells were treated with 1-200 μM cytarabine and cell viability was evaluated by MTT assay after 24, 48 and 72 h. Optical density was normalized to the control group, which was set at 100. Data are presented as the mean ± SD of three independent experiments.

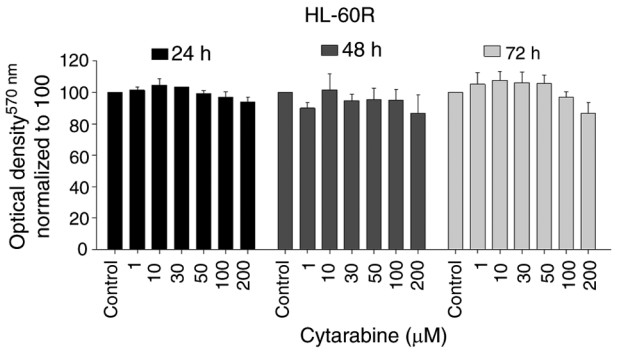

Figure S2. Cell cycle profile and DNA fragmentation remains unchanged after cytarabine treatment in HL-60R cells. Demonstrative histograms of (A) cell cycle distribution and (B) DNA fragmentation of HL-60 and HL-60R cells after treatment with 50 μM cytarabine for 48 h.

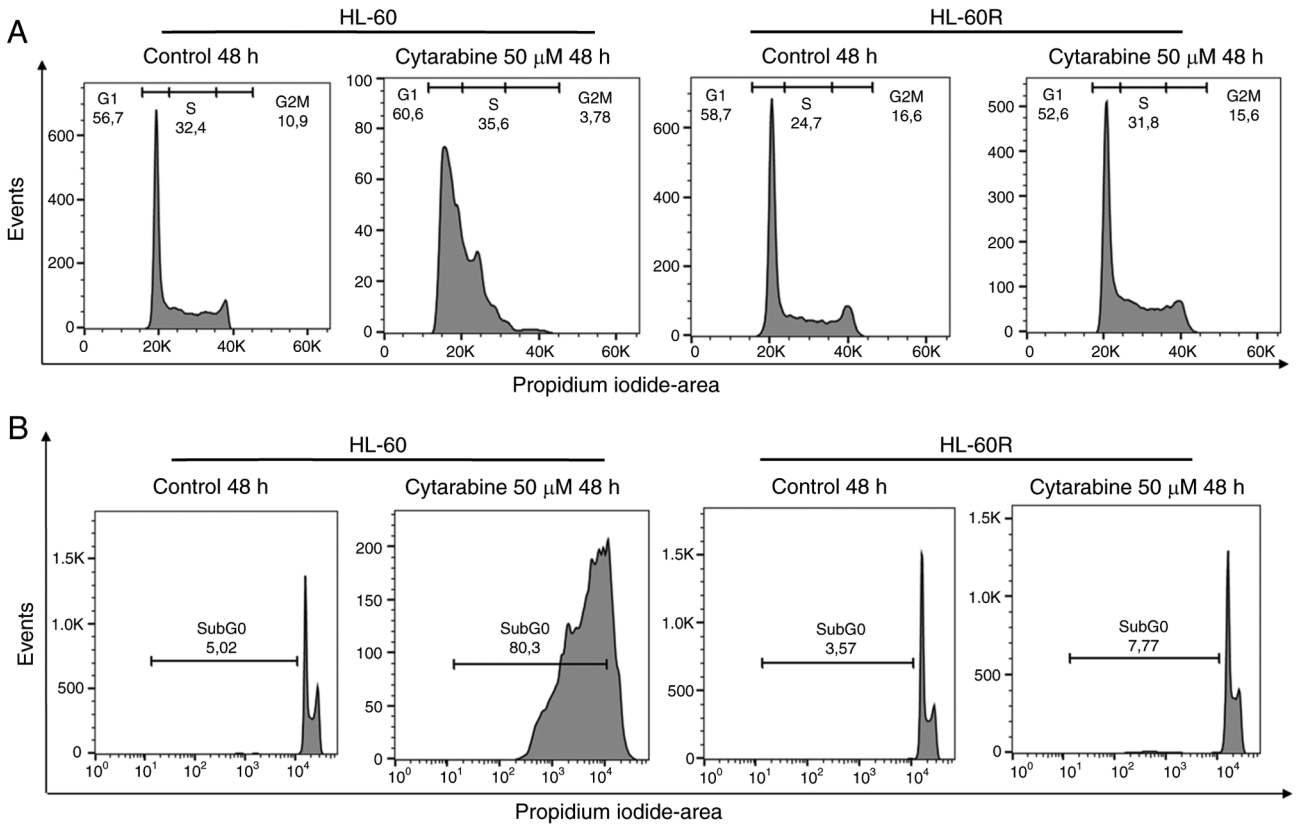

Figure S3. Cytarabine-resistant cells respond to anthracyclines used in AML treatment. Viability of HL-60 and HL-60R cells following treatment with idarubicin for (A) 24 h, (B) 48 h and (C) 72 h, and following treatment with daunorubicin for (D) 24 h, (E) 48 h and (F) 72 h, as determined by MTT assay. Optical density was normalized to the control group, which was set at 100. Data are presented as the mean ± SD of three independent experiments. Statistical significance was determined by Student's t-test. *P≤0.05.

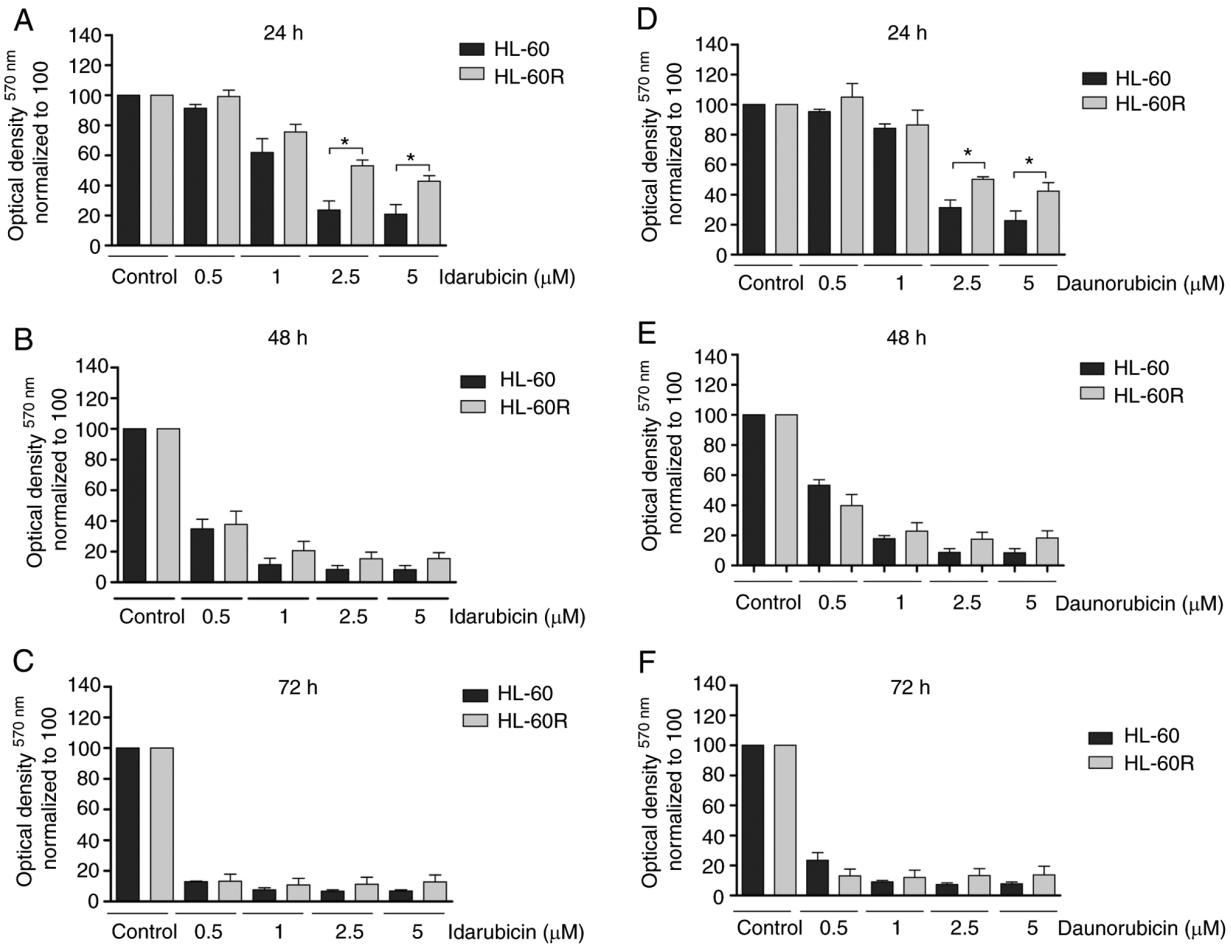

Figure S4. HL-60R cells possess a distinct karyotype to HL-60 cells. Karyotype analysis of the subpopulations of (A) HL-60 cells and (B) HL-60R cells after acquisition of resistance to cytarabine.

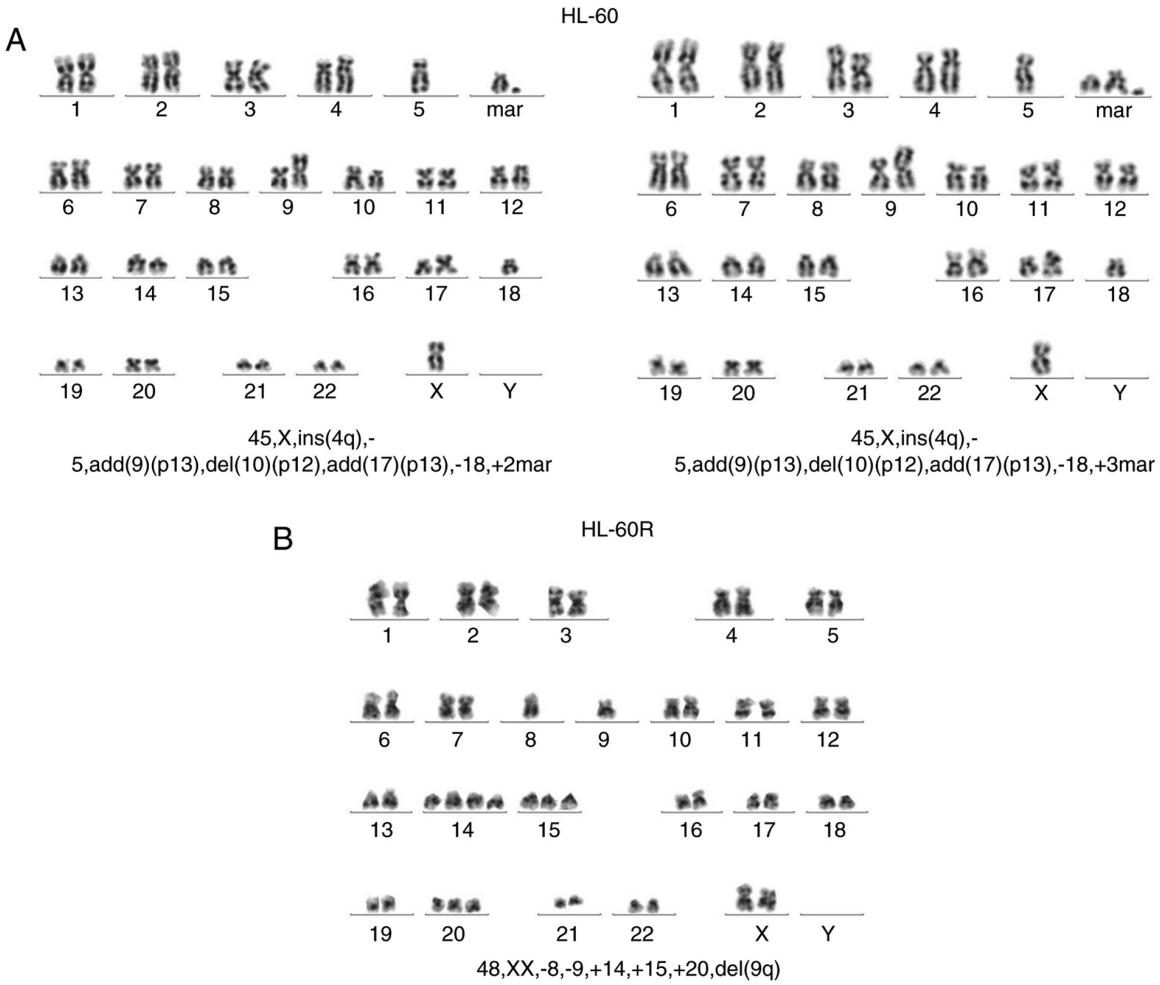

Figure S5. Mutation analysis in HL-60 and HL-60R cell lines. Upper panel, HL-60 and HL-60R cell lines were evaluated for *FLT3* internal tandem duplications and *NPM1* mutations by PCR using specific fluorescent primers, followed by fragment analysis. A fragment corresponding to WT *FLT3* (328 + 1 bp) or WT NPM1 (347 + 1 bp) was observed for HL-60 and HL-60R cell lines. Lower panel, *IDH1* exon 4, *IDH2* exon 4, *DNMT3A* exon 23 and *CEBPA* were analyzed by PCR and direct sequencing. No mutations in hot spots *IDH1* R132, *IDH2* R140 or *DNMT3A* R882 were observed for HL-60 or HL-60R cell lines. The *IDH1* c.315C>T p.Gly105Gly (rs11554137, heterozygous) and the *CEBPA* c.690G>T p.Thr230Thr (rs34529039, homozygous) synonymous variants were detected in both cell lines. WT, wild type.

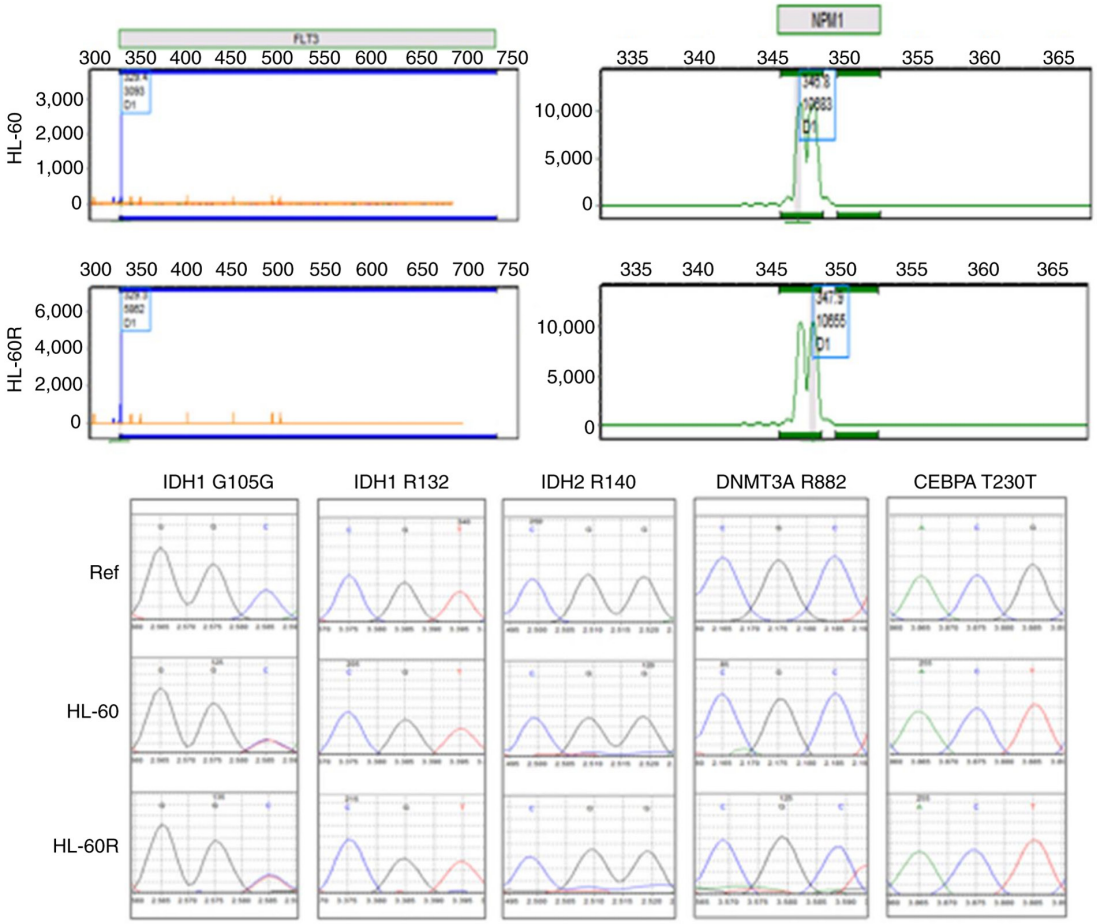

Figure S6. Mouse body weight and overall survival remains unchanged after cytarabine treatment *in vivo*. (A) Body weight over 15 days and (B) overall survival time of mice from each experimental group. Body weight data are presented as the mean ± SEM. Statistical significance was determined by (A) Student's t-test and (B) log-rank test.

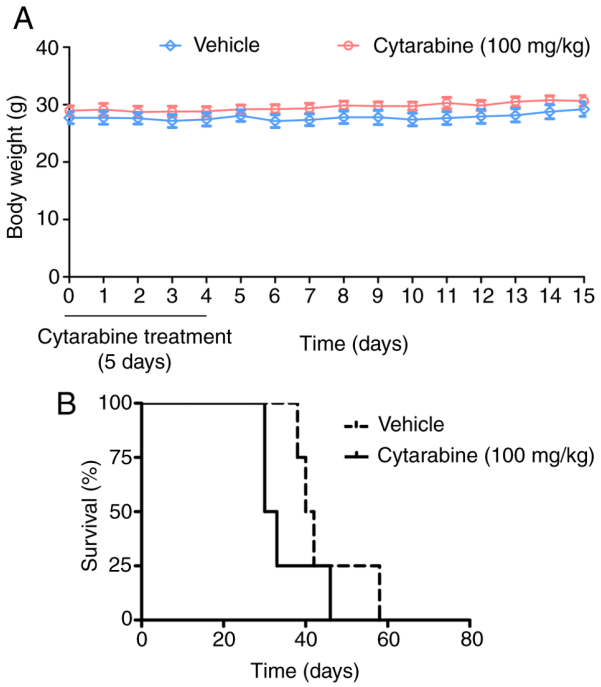

Figure S7. Relative mRNA expression levels of *MYC* in HL-60 and HL-60R cells, as determined by reverse transcription-quantitative PCR. mRNA expression levels were normalized to *β-actin*. Data are presented as the mean ± SD of three independent experiments.

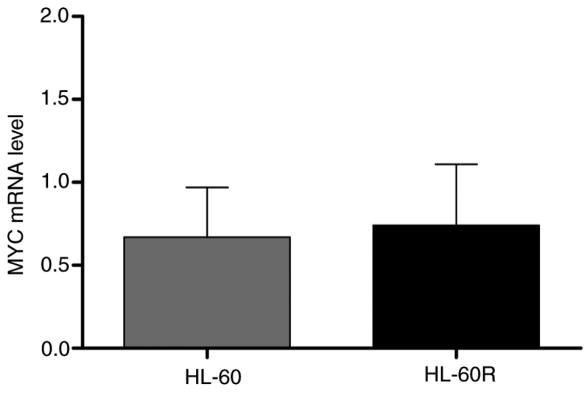

Table SI. Primer sequences used to evaluate *FLT3* ITDs, and *CEBPA*, *DNMT3A*, *IDH1*, *IDH2* and *NPM1* gene mutations.

Primer	Sequence
FLT3 ITD F	5'-TGTCGAGCAGTACTCTAAACA-3'
FLT3 ITD R	5'-FAM-ATCCTAGTACCTTCCCAAACTC-3'
NPM1 F	5'-ATCAATTATGTGAAGAATTGCTTAC-3'
NPM1 R	5'-HEX-ACCATTTCCATGTCTGAGCACC-3'
IDH1 exon4 F	5'-TGCCACCAACGACCAAGTCA-3'
IDH1 exon 4 R	5'-TGTGTTGAGATGGACGCCTATTTG-3'
IDH2 exon 4 F	5'-GGGGTTCAAATTCTGGTTGA-3'
IDH2 exon 4 R	5'-CTAGGCGAGGAGCTCCAGT-3'
CEBPA 1F	5'-GGCGAGCAGGGTCTCCGGGT-3'
CEBPA 1R	5'-TGTGCTGGAACAGGTCGGCCA-3'
CEBPA 2F	5'-GCTGGGCGGCATCTGCGA-3'
CEBPA 2R	5'-CCCCGACGCGCTCGTACAGG-3'
CEBPA 3F	5'-CCGGCTACCTGGACGGCAGG-3'
CEBPA 3R	5'-CGTTGCTGTTCTTGTCCACCGACTTCTT-3'
CEBPA 4F	5'-CTCGGTGCCGCCGGCCT-3'
CEBPA 4R	5'-AACCACTCCCTGGGTCCCCGC-3'
DNMT3A exon 23 F	5'-GTGTGGTTAGACGGCTTCCG-3'
DNMT3A exon 23 R	5'-CCCATGTCCCTTACACACACG-3'

F, forward; R, reverse; ITDs, internal tandem duplications.