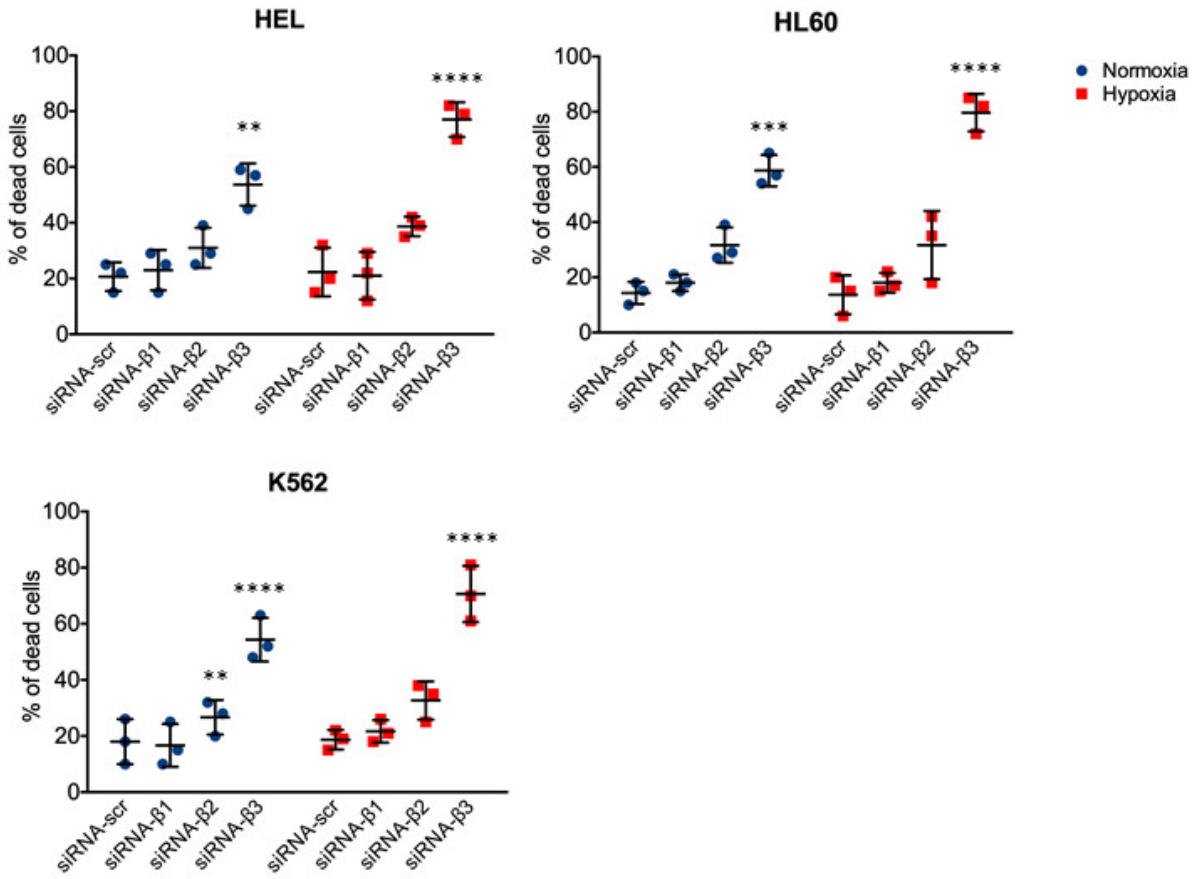
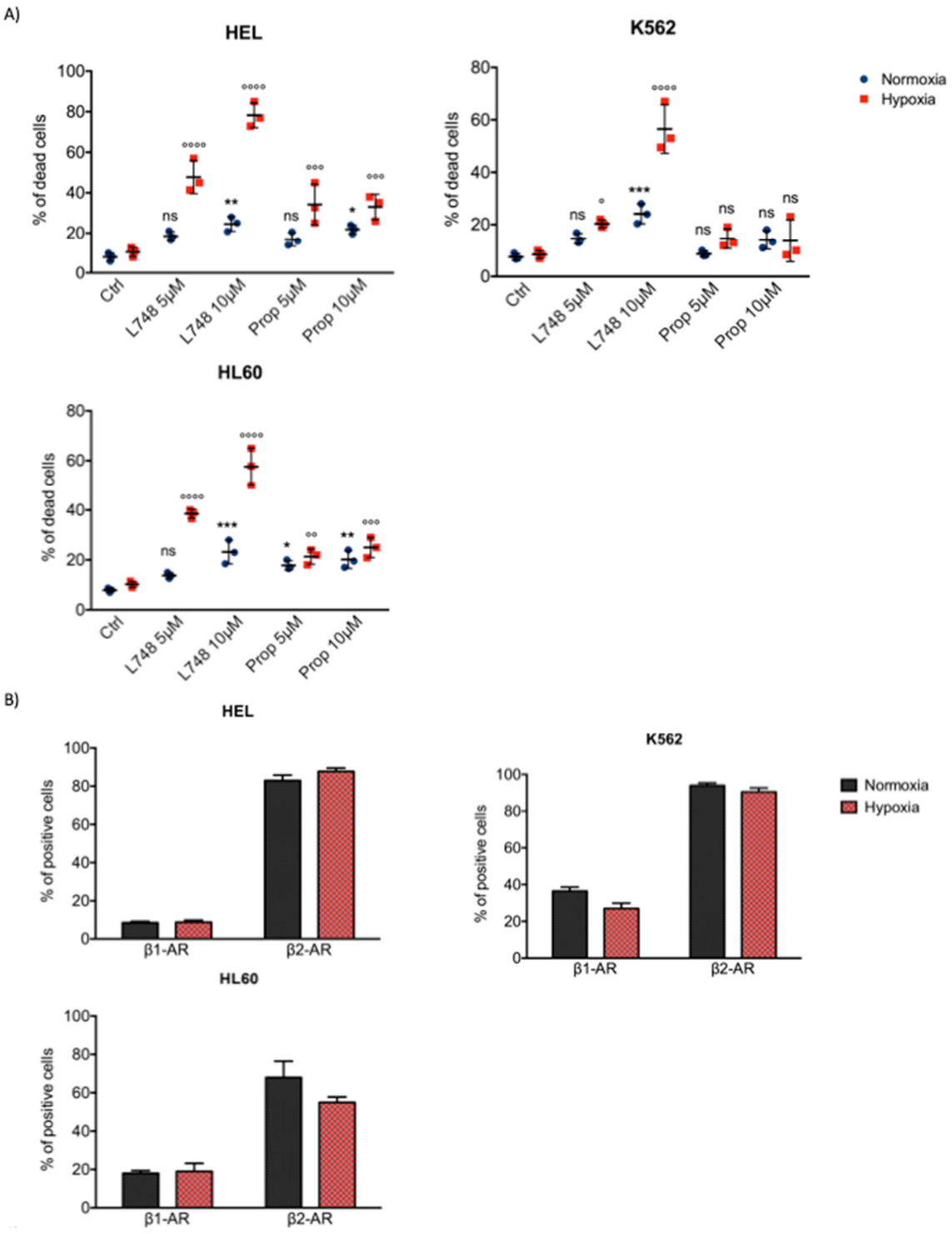
A)




B)

| | DOXO | DOXO + SR 3µM | DOXO + SR 5µM |
|---|---|---|---|
| IC50 Normoxia (µM) | 0.061 | 0.089 | 0.19 (1.4)* |
| IC50 Hypoxia (µM) | 0.27 | 0.04 (1.55)* | 0.019 (14.2)* |

**Supplementary Figure S1.** (**A**) Cell death assessment in myeloid leukemia cell lines silenced for β1-, β2- and β3-ARs in hypoxia and normoxia. Apoptosis evaluation through Annexin V and Propidium Iodide in HEL, K562, and HL60 cell lines transfected with selective siRNA for β1-, β2-, β3-ARs. (**B**) Average $IC_{50}$ values of doxorubicin and its combination with the SR59230A (referring to Figure 6B). The table also shows the RF (*reversal fold) value calculated from the ratio between the $IC_{50}$ value of doxorubicin in the absence of SR59230A and in the combination with the compound under study.




**Supplementary Figure S2.** (**A**) Cell death assessment in myeloid leukemia cell lines treated with L748,337 and Propranolol in hypoxia and normoxia. β-ARs blockers effects on HEL, K562 and HL60 leukemia cell lines. Apoptosis evaluation through Annexin V in HEL, K562 and HL60 cell lines treated with different concentration of L748,337 (5 µM, 10 µM) and Propranolol (5 µM, 10 µM) for 48 h, in normoxia (21% $O_2$) and in hypoxia (1% $O_2$); Significance was calculated by one-way ANOVA analysis followed by Bonferroni's post-hoc test. Results are reported as mean ± SD of three independent experiments. n = 3 per group. (*P < 0.05, **P < 0.01, ***P < 0.001 L748 or Prop vs. Ctrl Normoxia; °P < 0.05, °°P < 0.01, °°°P < 0.001, °°°°P < 0.0001 L748 or Prop vs. Ctrl Hypoxia). (**B**) β1- β2- and β3-ARs protein expression in myeloid leukemia cell lines in hypoxia and

normoxia. Evaluation of β1-AR and β2-AR positive cells in HEL, K562 and HL60 leukemia cell lines in normoxia and hypoxia.