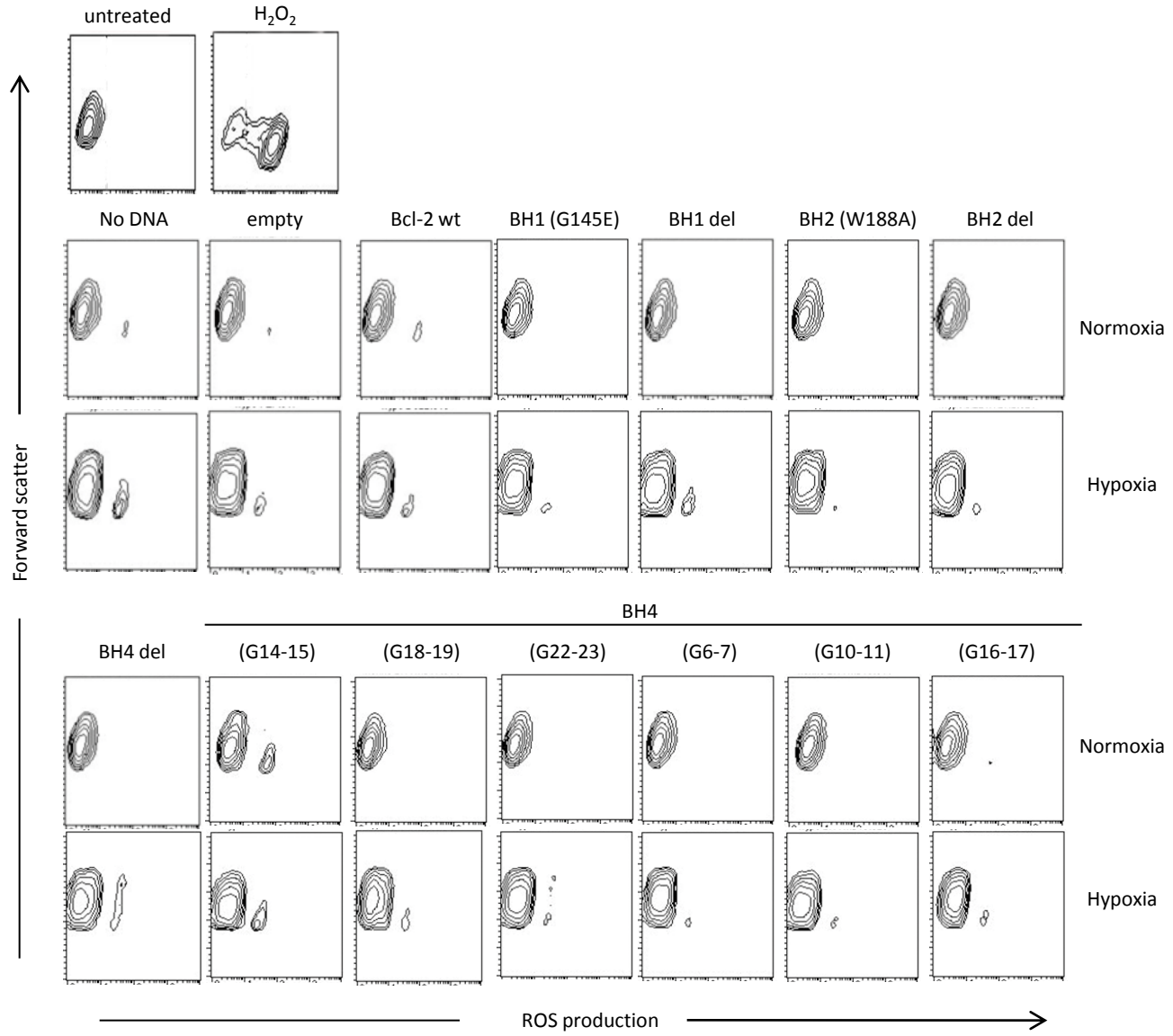
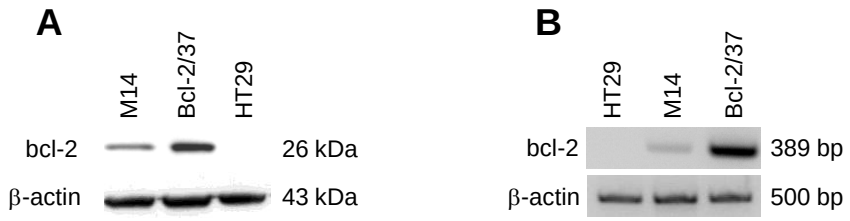
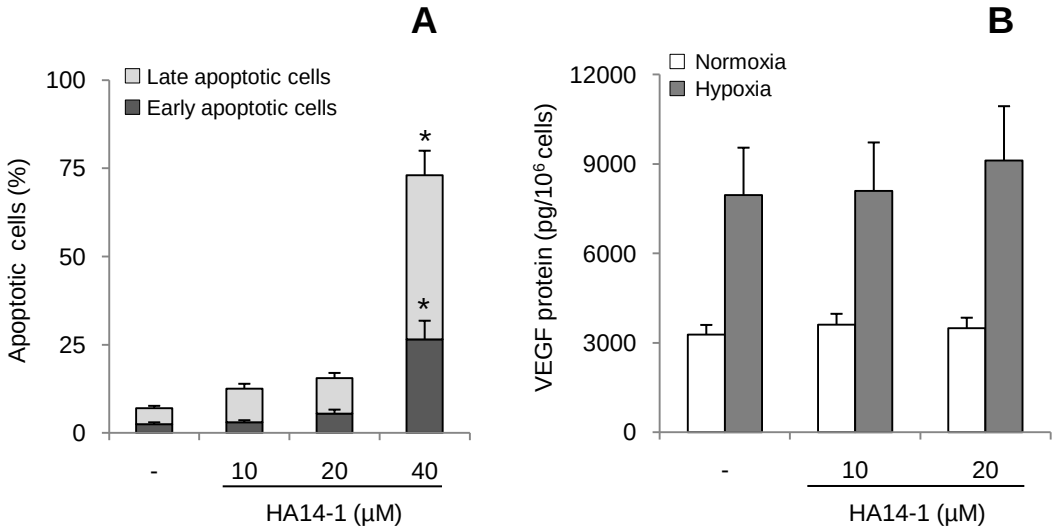


Supplementary Figure 1. Hypoxia does not induce reactive oxygen species (ROS) production. Flow cytometric analysis of ROS production performed on M14 cells untransfected (No DNA) or transiently transfected vectors encoding *wild type* or mutated bcl-2 protein, exposed to normoxia (untreated) or hypoxia for 24 h. Expressing vector encoding bcl-2 *wild type* (Bcl-2 wt) or point mutants at the BH1 (G145E) and the BH2 (W188A), into the BH4 (G14-15, G18-19, G22-23, G6-7, G10-11, G16-17) domain, and bcl-2 deleted of the BH4 (BH4 del), BH1 (BH1 del) and BH2 (BH2 del) domains were used. The untransfected (No DNA) and the control vector transfected (empty) M14 cells were used as control. Briefly 5 x 10^5 adherent cells were incubated with 4 μM dihydroethidium (DHE; Molecular Probes, Eugene, OR) for 45 minutes at 37°C in PBS. The data are presented as biparametric panels of the DHE fluorescence intensity (FL-2) *versus* the forward scatter. Each panel is representative of two separate experiments with comparable results.



Supplementary Figure 2. HT29 cell line is deficient for bcl-2 expression. Western blot analysis of protein expression **(A)** and RT-PCR evaluation of mRNA level **(B)** of bcl-2 in HT29 human colon carcinoma cell line, M14 human melanoma cell line and its derivative bcl-2 overexpressing clone Bcl2/37. **(A)** Western blots representative of three independent experiments with similar results are shown. β-actin protein expression is shown as loading and transferring control. **(B)** 2µl cDNA were added to PCR reaction mix containing exon-specific primers targeting bcl-2 (sense CGACTTCGCCGAGATGTCCAGCCA, antisense ACTTGTGGCCCAGATAGGCACCCA) for 32 cycles with an annealing temperature of 65°C. β-actin mRNA expression was used as control.



Supplementary Figure 3. Small-molecule HA14-1, an inhibitor of bcl-2, does not affect VEGF protein expression in stable Bcl-2 overexpressing cells. **(A)** Flow cytometric evaluation of Annexin V^+/PI^- (early apoptotic cells) and Annexin V^+/PI^+ (late apoptotic cells) cells evaluated in *wild type* bcl-2 overexpressing clone Bcl-2/6 exposed to doses of HA14-1 ranging from 10 to 40µM for 24 h. Percentages of apoptotic cells were calculated by Cellquest software. **(B)** VEGF protein expression evaluated by ELISA in *wild type* bcl-2 overexpressing clone Bcl-2/6 treated with 10 and 20µM doses of HA14-1 in normoxic or hypoxic conditions for 24 h. **(A,B)** Results represent the average ± SD of three independent experiments. p values were calculated between untreated and treated cells (*$p<0.01$).