

Figure S1. The transcriptional profile following MBZ treatment is similar across six cancer cell lines and includes HIF-inhibitors. Heatmap of well-annotated small molecular perturbations that result in a similar transcriptomic profile as MBZ treatment in a core set of 6 cancer cell lines using the *Touchstone v1 dataset*.

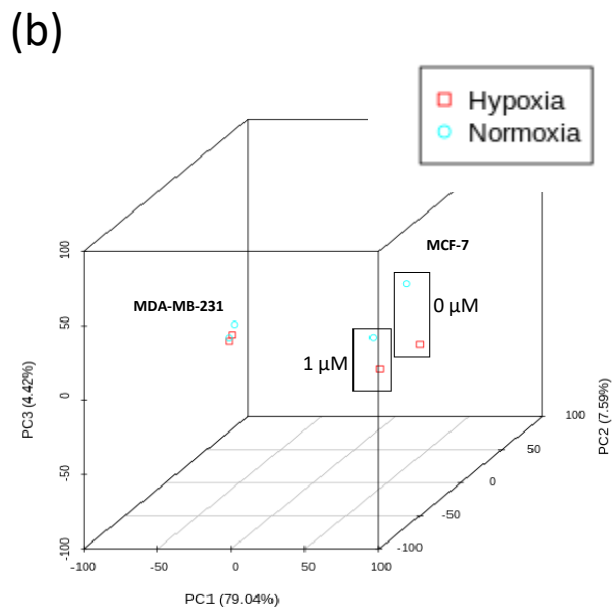
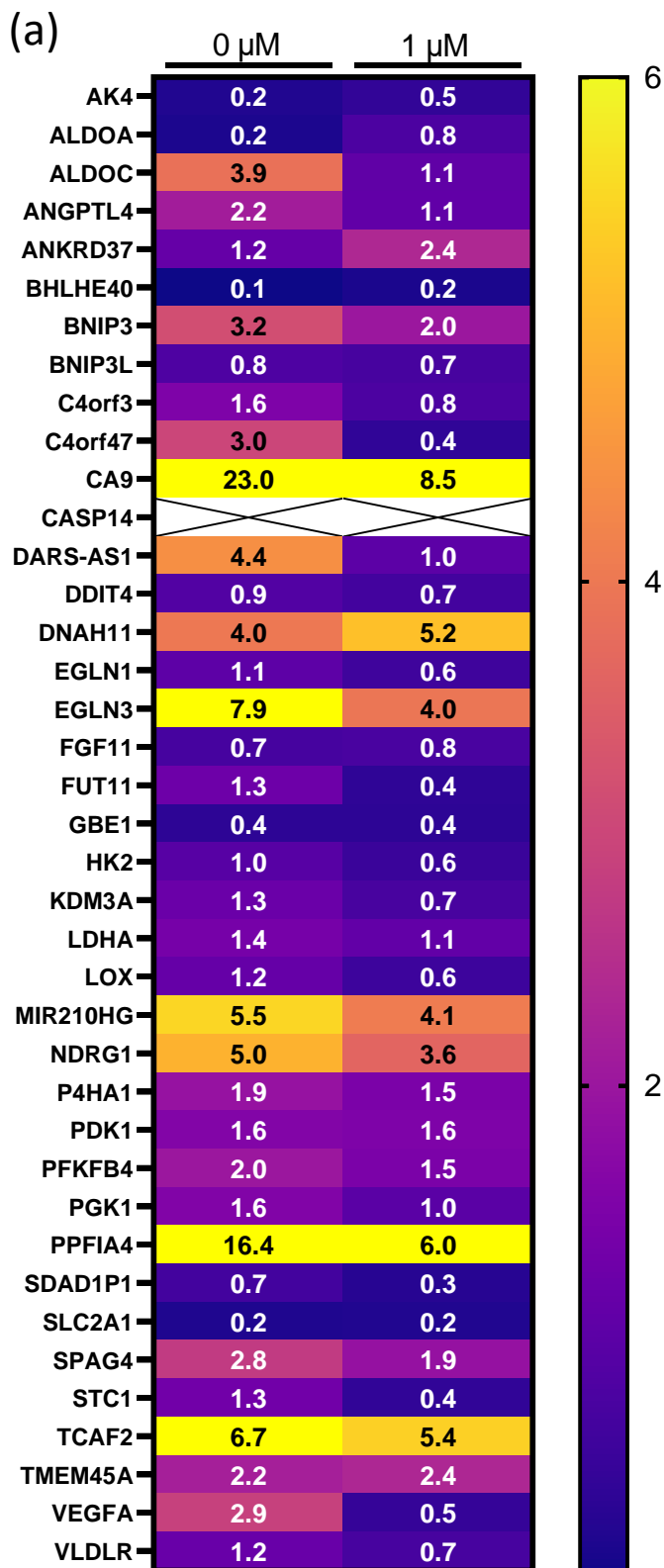


Figure S2. *Mebendazole decreases the hypoxia-induced expression of a 42-gene hypoxia breast cancer signature in MDA-MB-231 cells* (a) Heatmap of the fold change in gene expression values for the 42-gene hypoxia signature in MDA-MB-231 cells treated in the presence (1 μ M) or absence (0 μ M) of MBZ under 1% versus 20% O₂ conditions. (b) 3D PCA plot of MDA-MB-231 or MCF-7 gene expression in the presence (1 μ M) or absence (0 μ M) of MBZ and exposed to 1% or 20% O₂ conditions.

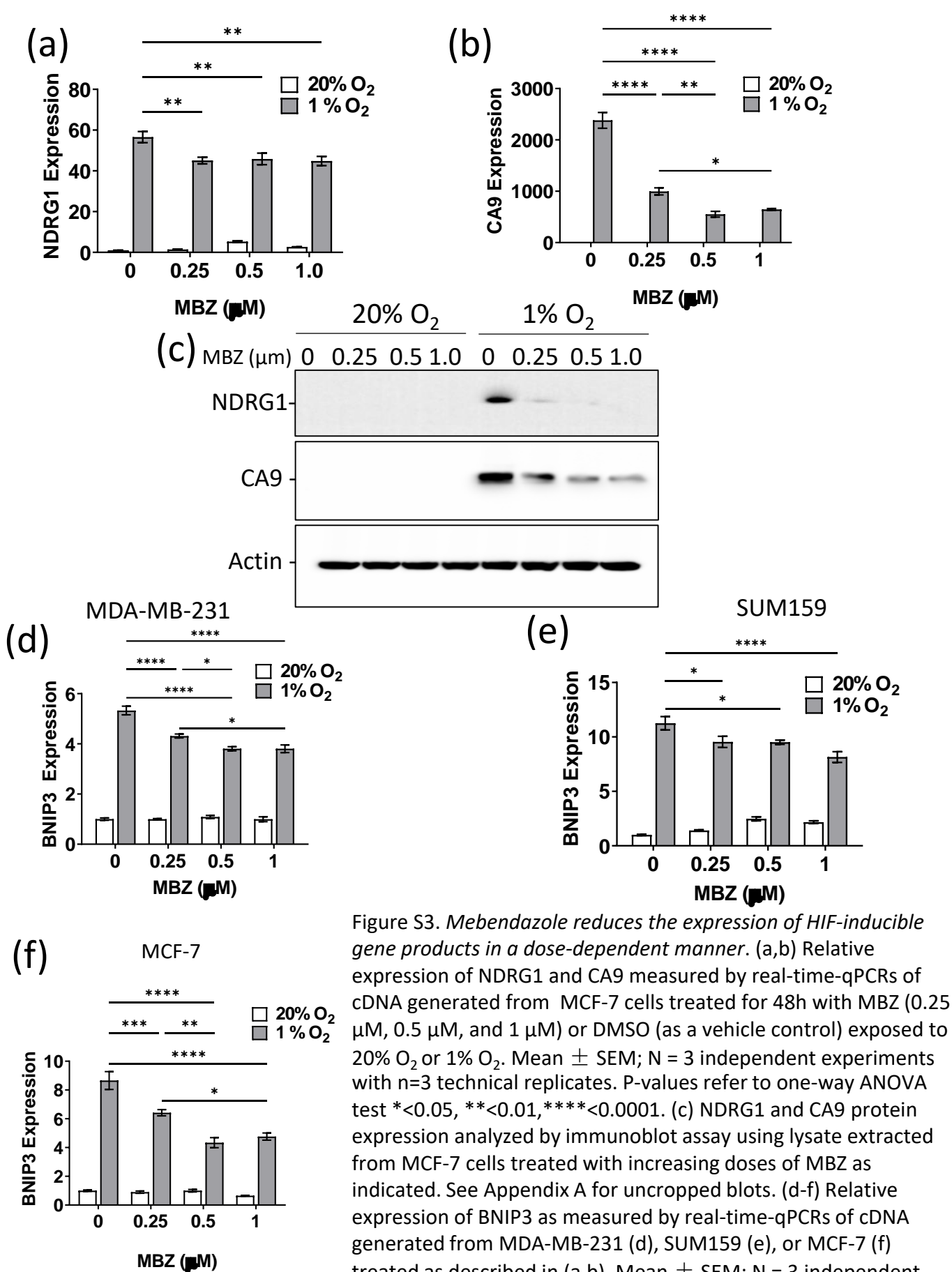


Figure S3. *Mebendazole reduces the expression of HIF-inducible gene products in a dose-dependent manner.* (a,b) Relative expression of NDRG1 and CA9 measured by real-time-qPCRs of cDNA generated from MCF-7 cells treated for 48h with MBZ (0.25 μM , 0.5 μM , and 1 μM) or DMSO (as a vehicle control) exposed to 20% O_2 or 1% O_2 . Mean \pm SEM; N = 3 independent experiments with n=3 technical replicates. P-values refer to one-way ANOVA test * <0.05 , ** <0.01 , **** <0.0001 . (c) NDRG1 and CA9 protein expression analyzed by immunoblot assay using lysate extracted from MCF-7 cells treated with increasing doses of MBZ as indicated. See Appendix A for uncropped blots. (d-f) Relative expression of BNIP3 as measured by real-time-qPCRs of cDNA generated from MDA-MB-231 (d), SUM159 (e), or MCF-7 (f) treated as described in (a,b). Mean \pm SEM; N = 3 independent experiments with n=3 technical replicates. P-values refer to one-way ANOVA test * <0.05 , ** <0.01 , *** <0.001 , **** <0.0001 .

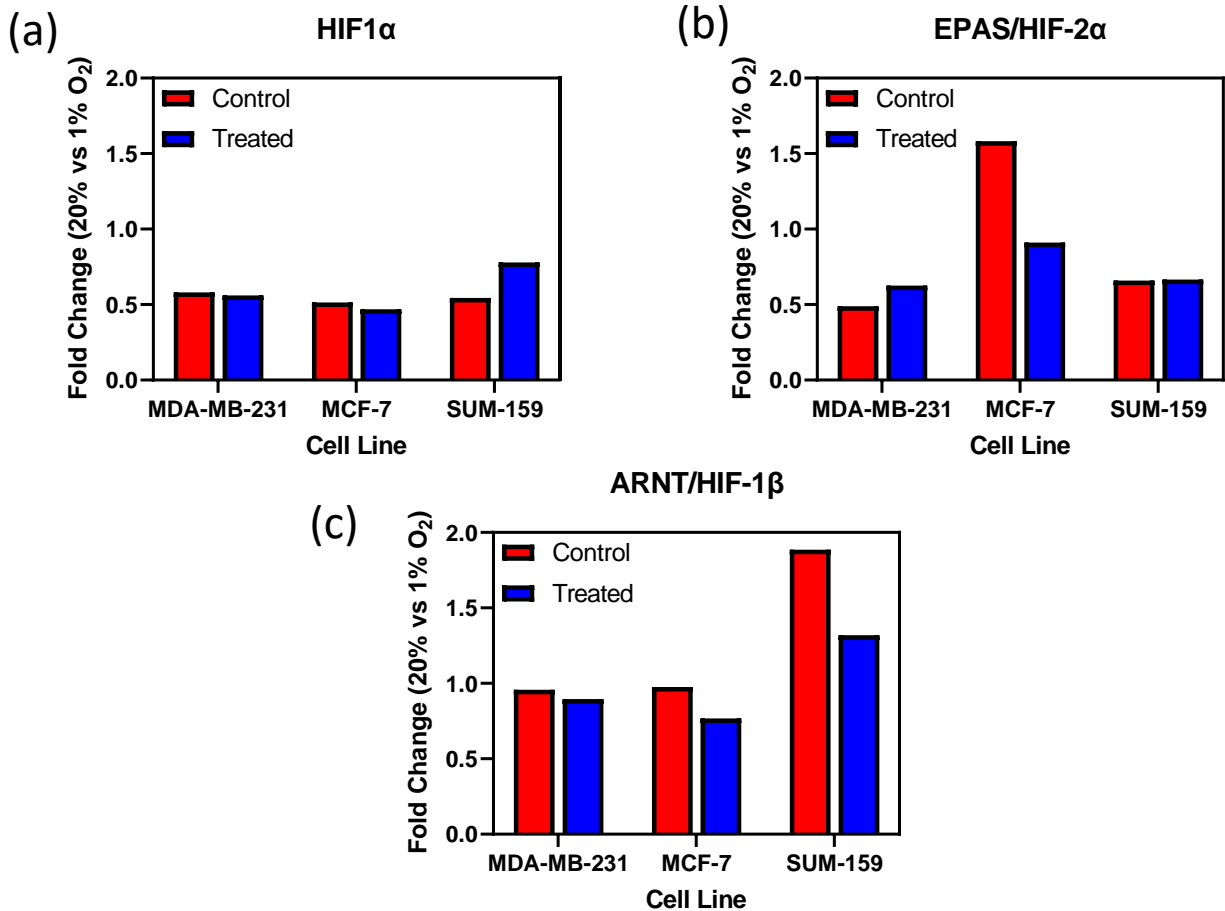


Figure S4. *Mebendazole does not significantly alter the mRNA expression of the HIF1, EPAS/HIF-2 α , or ARNT/HIF-1 β genes;.* The fold change of the normalized counts for the *HIF-1* (a) gene which encodes HIF-1 α , *EPAS* (b) gene which encodes HIF-2 α , or the *ARNT* (c) gene that encodes HIF-1 β obtained by RNA sequencing data and quantified for MDA-MB-231, MCF-7, or SUM159 cells treated with DMSO as a vehicle control (control) or 1 μ m of MBZ (treated).