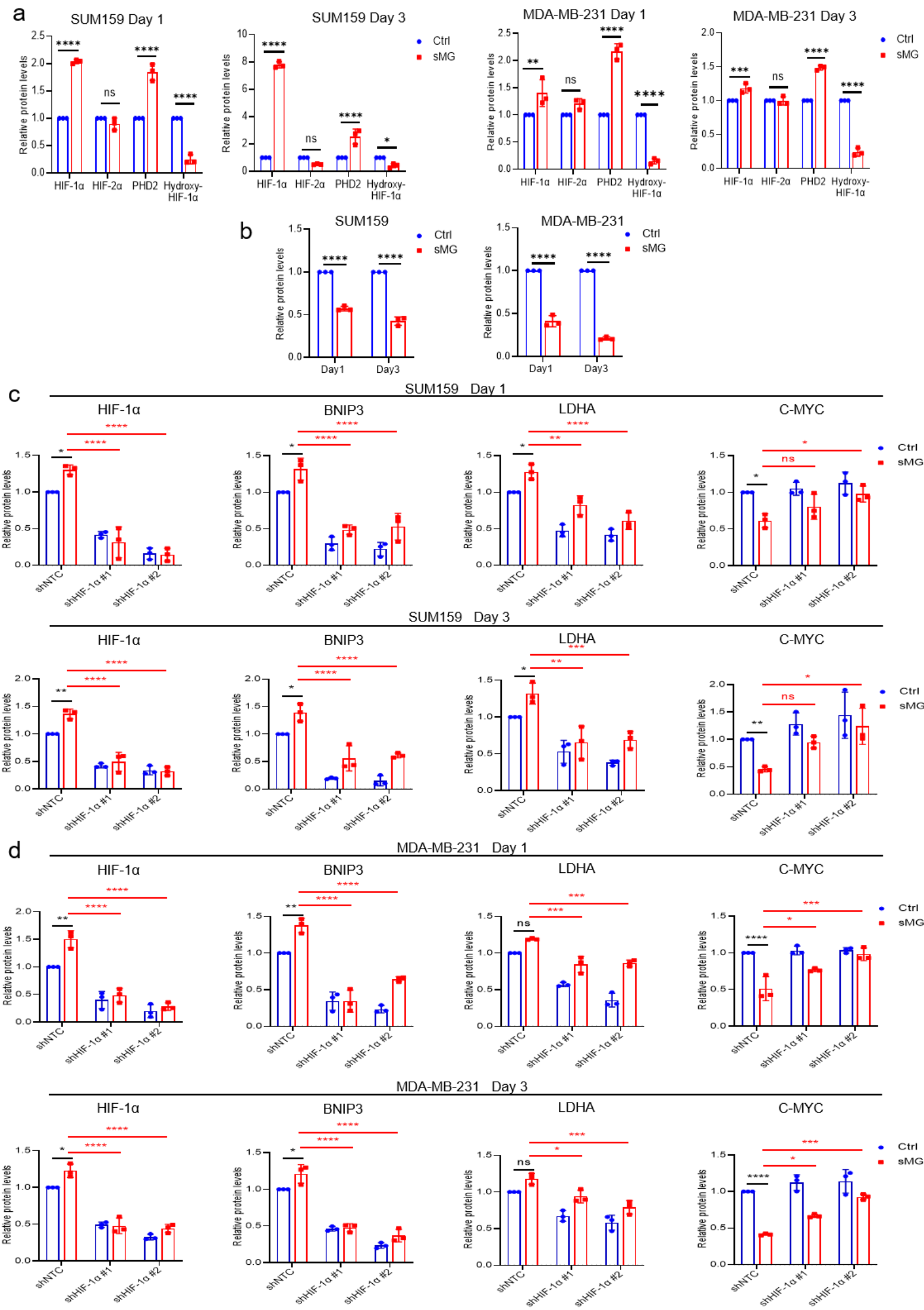


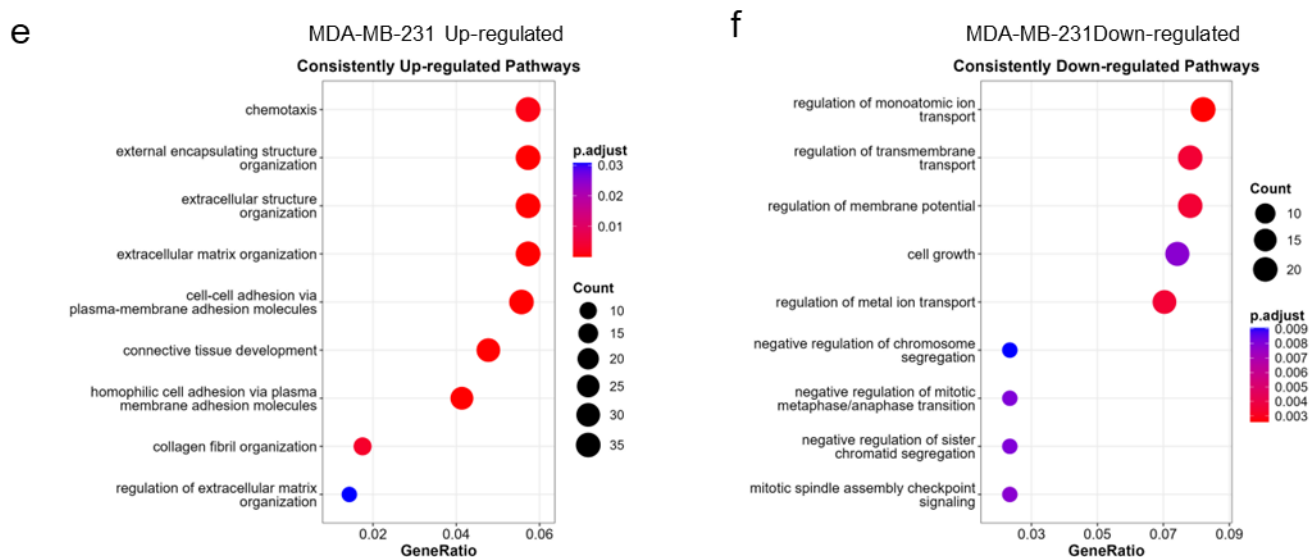
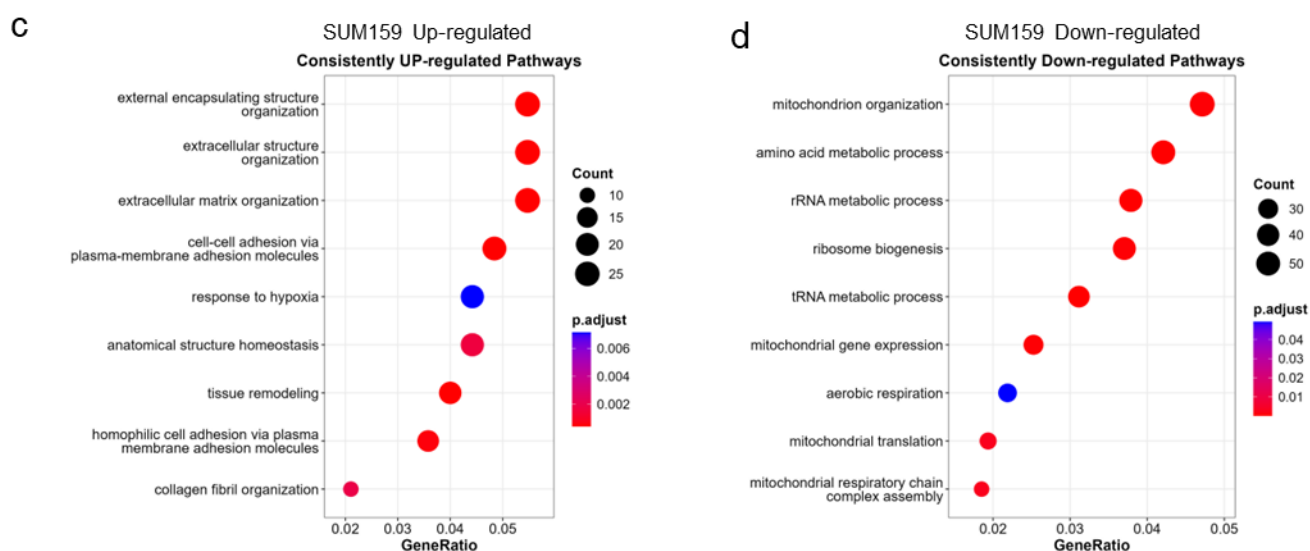
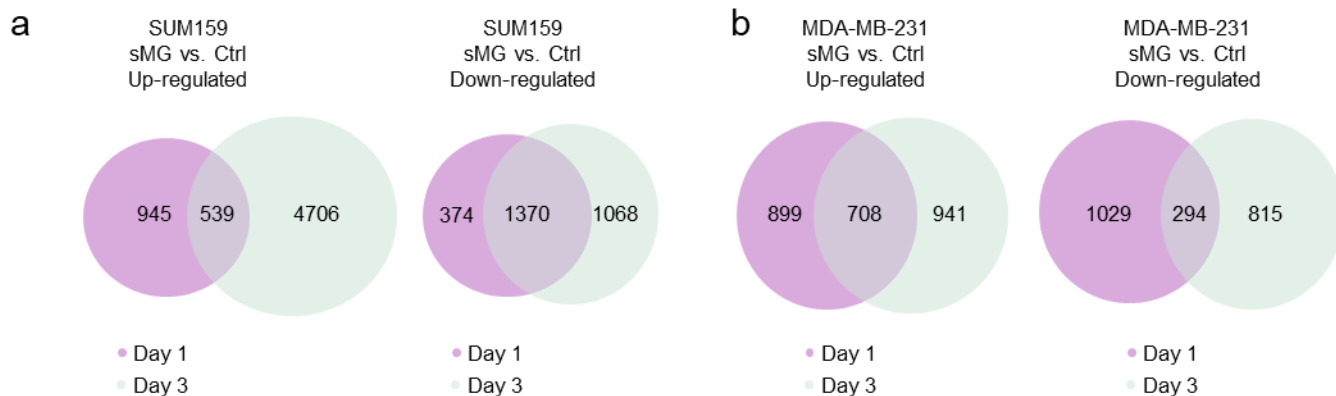


Supplementary Figure S1. Densitometric quantification of Western blots.

(a, b) Relative protein levels of HIF-1 α , HIF-2 α , Hydroxy-HIF-1 α , PHD2 (a) and c-MYC (b) in wild-type SUM159 and MDA-MB-231 cells under standard 1g (Ctrl) or sMG conditions for 1 and 3 days.

(c, d) Relative protein levels of HIF-1 α , BNIP3, LDHA, and c-MYC in control (shNTC) and HIF-1 α knockdown (shHIF-1 α #1/2) subclones of SUM159 (c) and MDA-MB-231 (d) under Ctrl or sMG conditions.

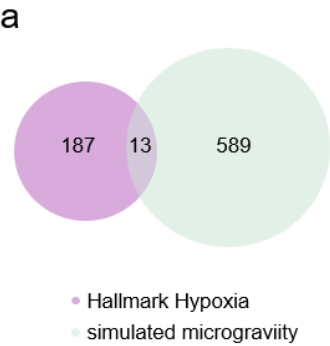
ImageJ-quantified data were normalized to the respective time-matched Ctrl groups (set to 1). Data are presented as mean $\pm$ SD (n = 3). *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001; ns, not significant. Black lines denote baseline sMG effects (Ctrl vs. sMG); red lines denote phenotypic rescue effects under sMG (shNTC vs. shHIF-1 α under sMG).



Supplementary Figure S2. Transcriptomic analysis of persistently altered genes in TNBC cells during prolonged sMG exposure.

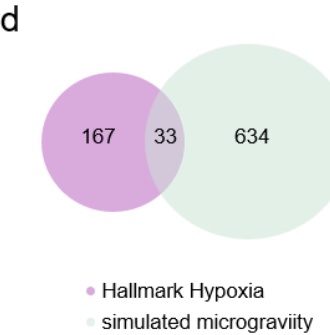
(a and b) Venn diagrams illustrating the overlap of consistently upregulated (left) and downregulated (right) differentially expressed genes (DEGs) between Day 1 and Day 3 of sMG exposure in SUM159 (a) and MDA-MB-231 (b) cells.

(c–f) Gene Ontology (GO) enrichment analyses of these temporally conserved DEGs, showing the top enriched biological process terms for persistently upregulated (c, e) and downregulated (d, f) genes in SUM159 (c, d) and MDA-MB-231 (e, f) cells, respectively.



b

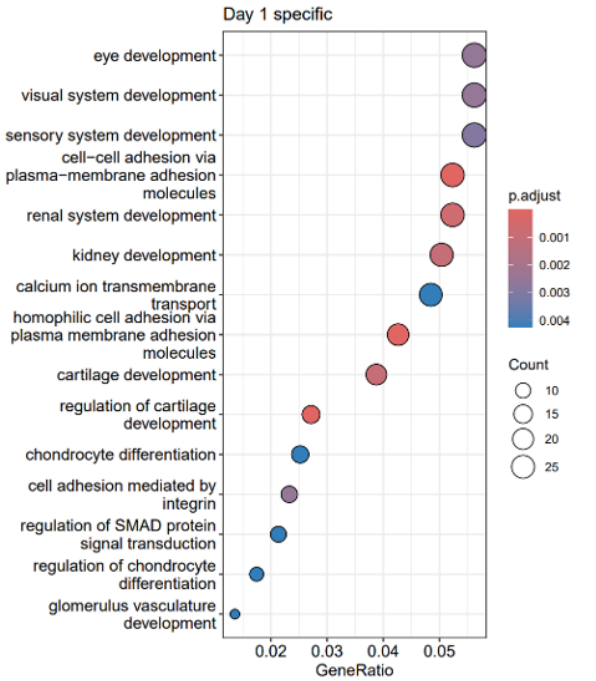
Functional Category	Commonly Activated Genes
Acute Metabolism & Energy Sensing	<i>SLC2A3, ATP7A, PPARGC1A</i>
Oxidative Stress & Detoxification	<i>HMOX1, GLRX</i>
Early Matrix Response & Microenvironment	<i>ANGPTL4, LOX, SDC2</i>
Cell Cycle Arrest & Transcription	<i>CDKN1A, CCNG2, BHLHE40, PNRC1, KLHL24</i>



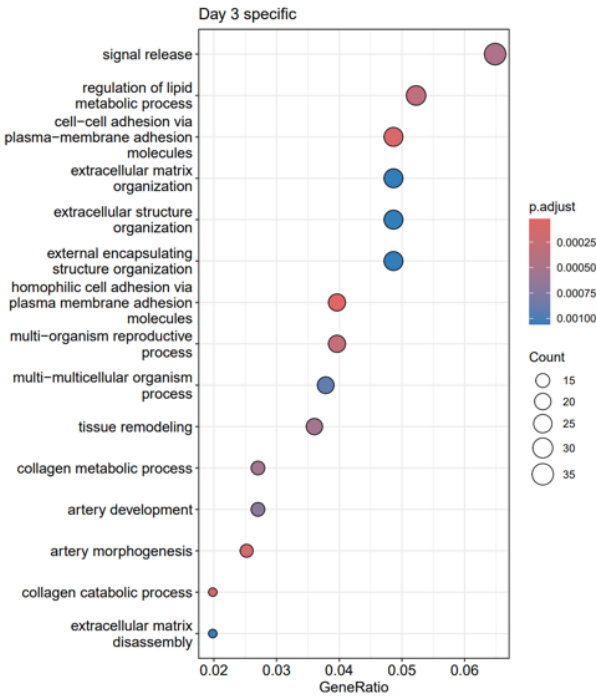
e

Functional Category	Commonly Activated Genes
Deep Metabolic Reprogramming	<i>SLC2A3, ALDOC, SLC2A5, SLC6A6, PLIN2, HEXA, AMPD3, ATP7A, CP</i>
Stress Response, Growth Suppression & Transcription	<i>NDRG1, CDKN1A, CCNG2, CCN5, BTG1, IGFBP3, BHLHE40, RORA, PPFIA4, TPBG, VLDLR, TMEM45A, PAM</i>
Angiogenesis & Matrix Remodeling	<i>VEGFA, ANGPTL4, SERPINE1, LOX, P4HA1, P4HA2, COL5A1, DCN, TGFB1, CA12, ACKR3</i>

c



f



Supplementary Figure S3. Comparative transcriptomic analysis between sMG-induced specific signature and the classical Hallmark Hypoxia response.

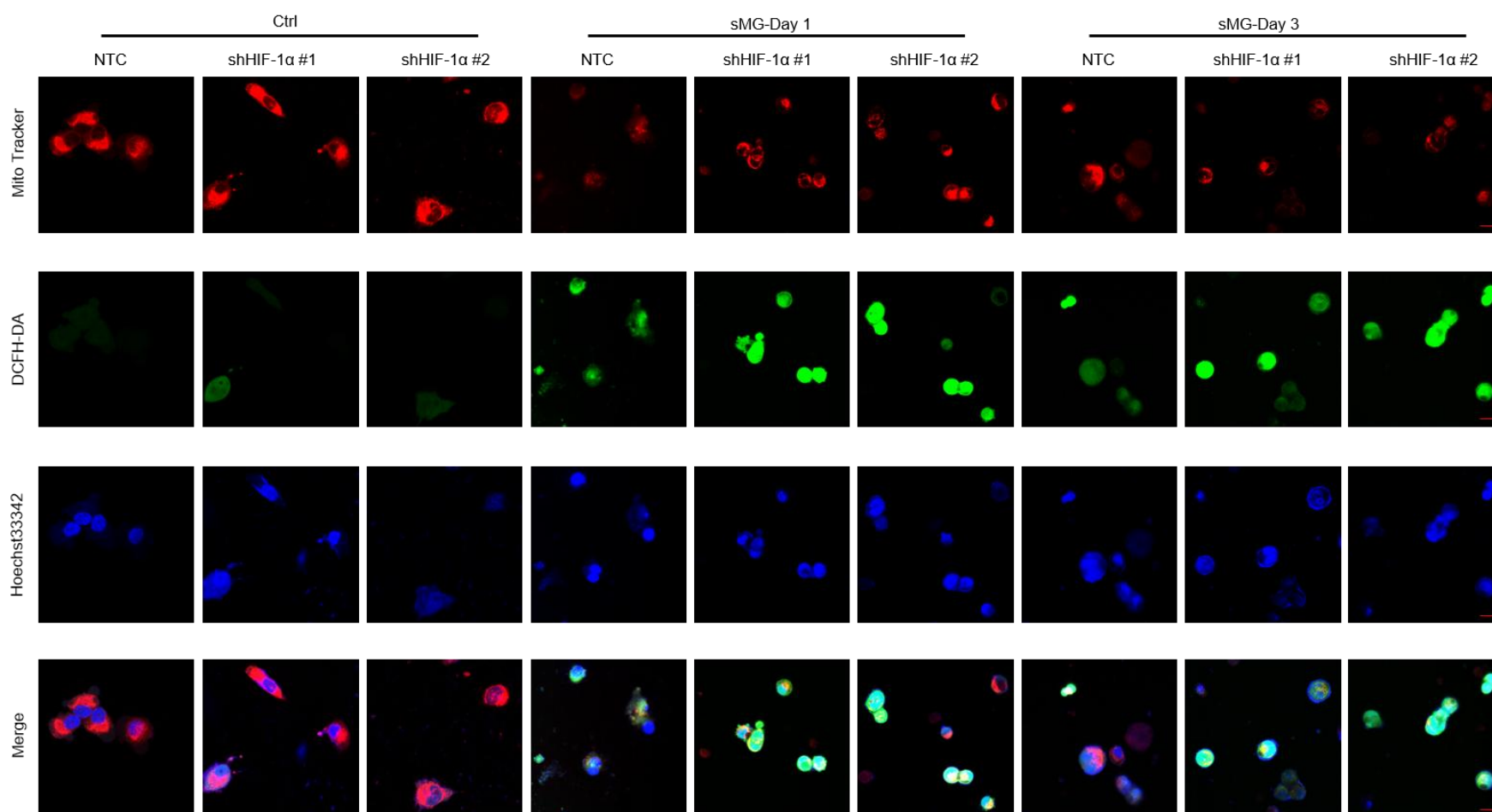
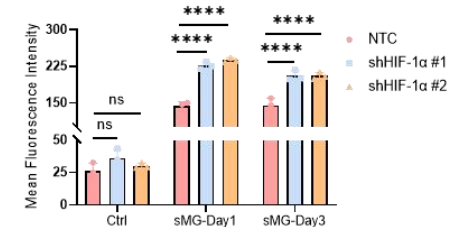
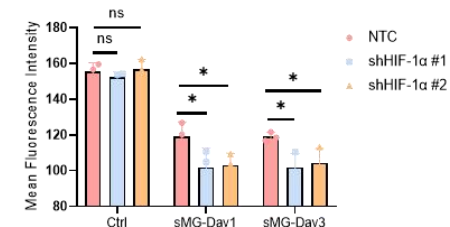
(a and d) Venn diagrams showing the intersection of consensus upregulated genes under sMG (shared by SUM159 and MDA-MB-231) and the MSigDB Hallmark Hypoxia gene set at Day 1 (a) and Day 3 (d).

(b and e) Functional categorization of the commonly upregulated genes shared between the sMG response and the Hallmark Hypoxia gene set at Day 1 (b) and Day 3 (e).

(c and f) Gene Ontology (GO) enrichment analysis (Biological Process) of the sMG-exclusive upregulated genes (**589** genes at Day 1; **634** genes at Day 3).

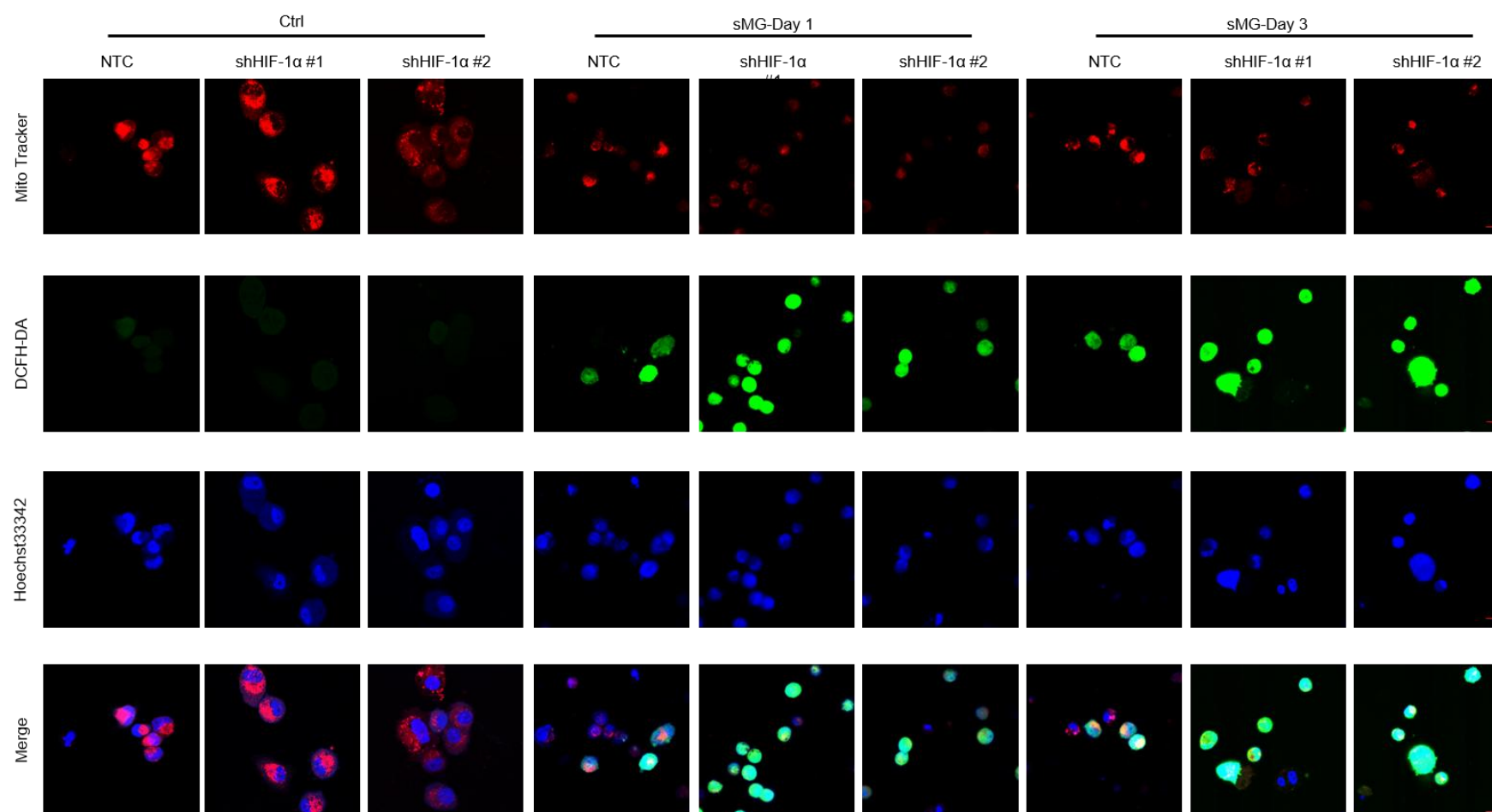
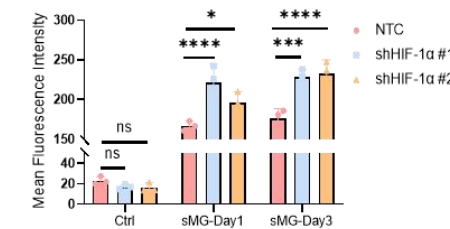
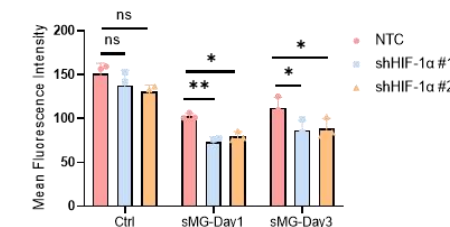
SUM159

a

b SUM159
DCFH-DA intensityc SUM159
MitoTracker intensity

MDA-MB-231

d

e MDA-MB-231
DCFH-DA intensityf MDA-MB-231
MitoTracker intensity

Supplementary Figure S4. Knockdown of HIF-1 α exacerbates sMG-induced ROS accumulation and mitochondrial dysfunction in TNBC cells.

(a and d) Representative confocal microscopy images assessing mitochondrial membrane potential (MitoTracker Red CMXRos) and intracellular ROS (DCFH-DA) in NTC and HIF-1 α knockdown SUM159 **(a)** and MDA-MB-231 **(d)** cells cultured under normal gravity (Ctrl) or sMG conditions for 1 and 3 days. Nuclei were counterstained with Hoechst 33342. Scale bars = 20 μ m.

(b, c, e, and f) Corresponding quantitative analysis of mean fluorescence intensity for DCFH-DA **(b, e)** and MitoTracker **(c, f)**. Data are presented as mean $\pm$ SD (n = 3). ns, not significant; *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.