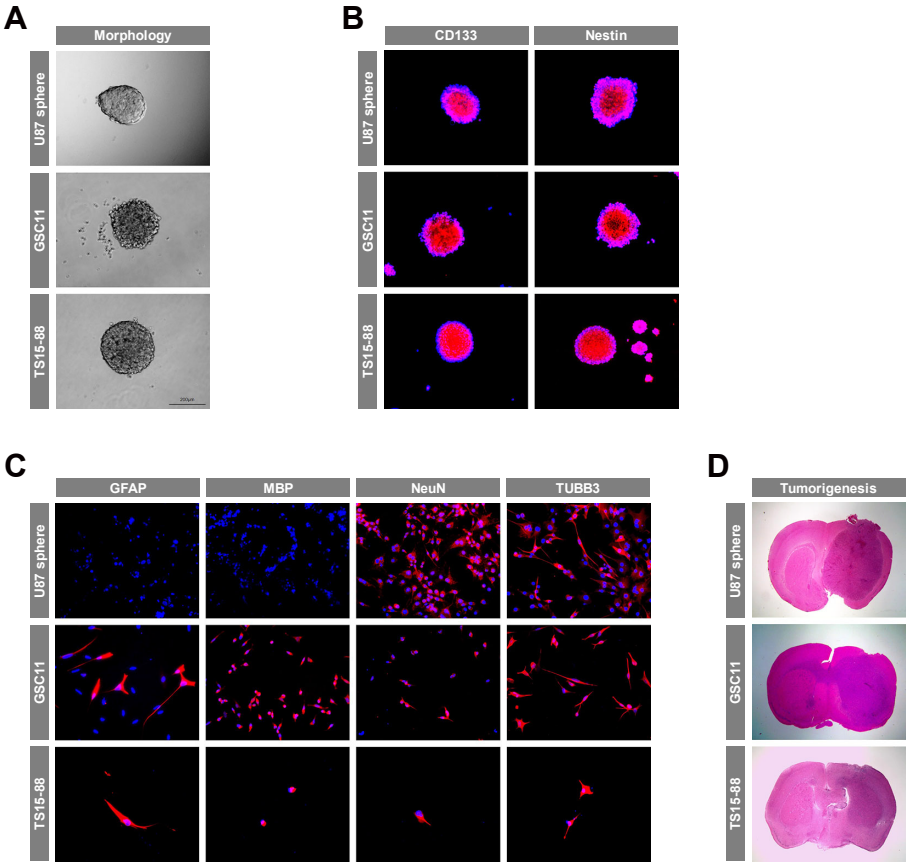
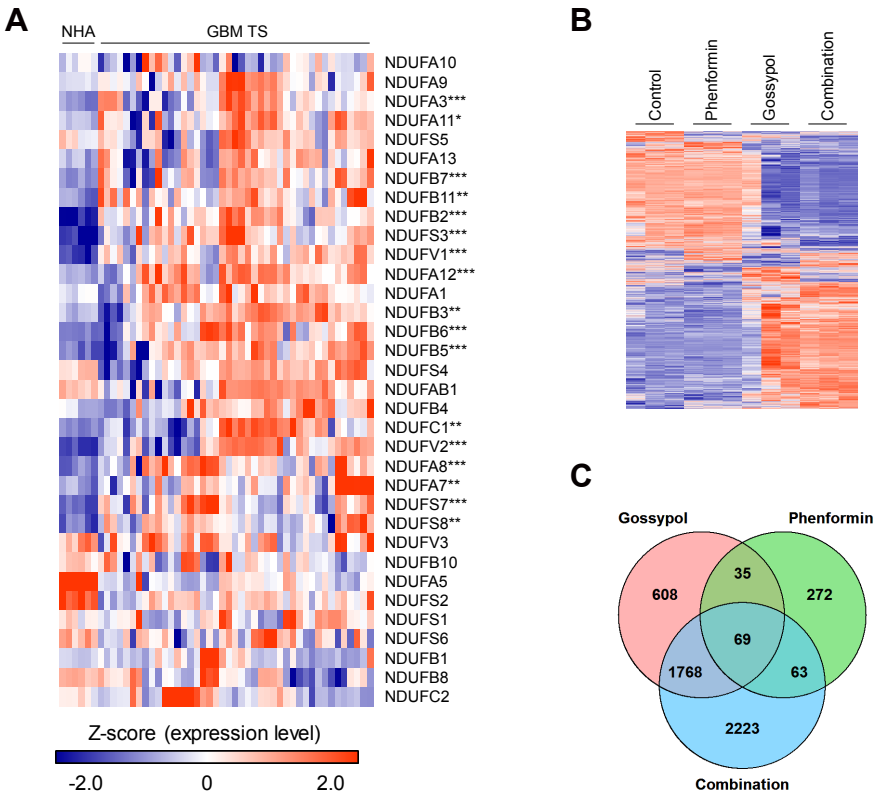
Supplementary Figures



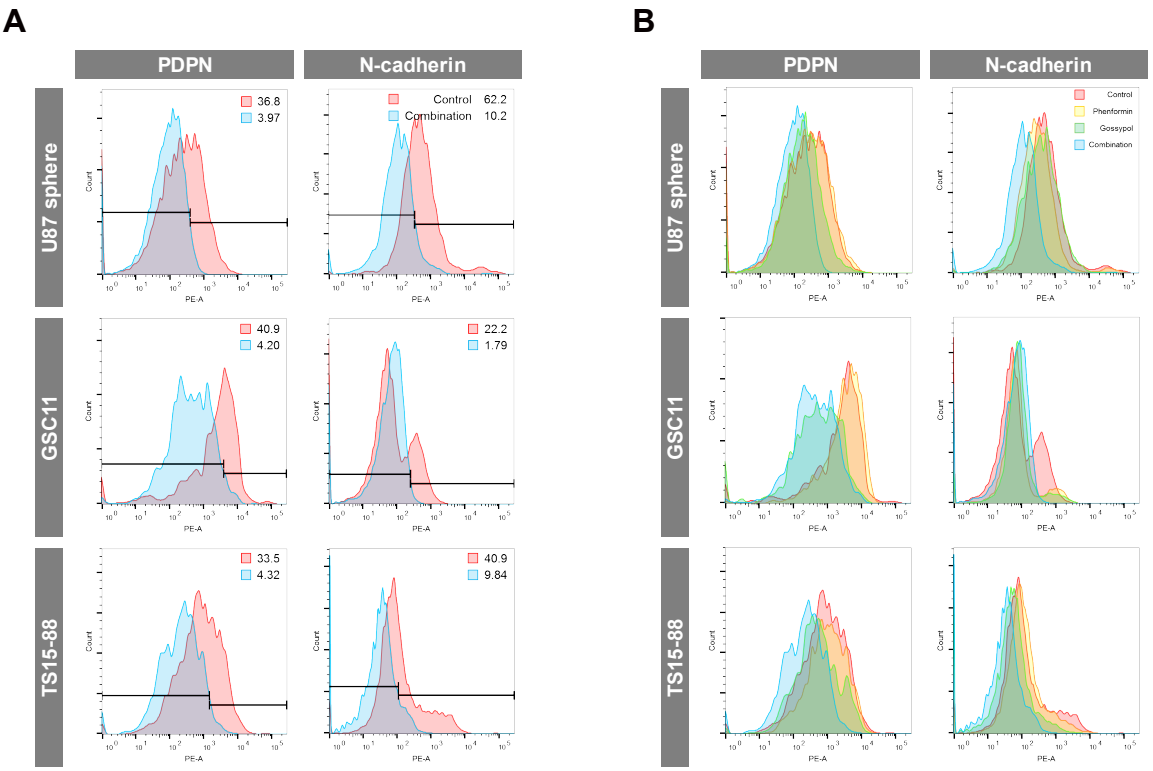
Supplementary Fig. S1. Characterization of GBM TSs (U87, GSC11, and TS15-88).

(A) Observation of sphere formation. (B, C) Expression levels of CD133 and Nestin (stemness markers, B), and GFAP, MBP, NeuN, and TUBB3 (neuroglial differentiation markers, C) were detected by immunocytochemistry (red). Nuclei were counterstained with DAPI (blue). (D) Tumorigenesis of each GBM TS was confirmed by a mouse orthotopic xenograft model with an injection of 2×10^5 cells. H&E staining shows tumor mass in the right frontal lobe of mice.



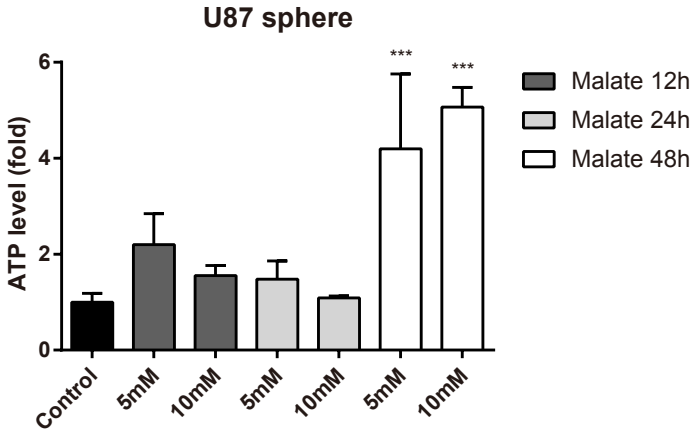
Supplementary Fig. S2. Analysis of gene expression profile.

(A) Expression levels of mitochondrial complex I-related genes were evaluated using Yonsei microarray dataset (NHA, n = 6; GBM TS, n = 43). Expression levels are presented as a heat map, and asterisks indicate significantly overexpressed genes (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ after FDR correction; two-tailed Student's *t*-test). (B) U87 spheres were treated with gossypol and phenformin alone or in combination for 72 h, and microarray data were obtained. Expression levels of all perturbed genes by treatment with gossypol and phenformin were displayed as a heat map. Differences among groups were compared by one-way ANOVA with Tukey's *post hoc* test for multiple comparisons, and perturbed genes were defined as those with $P < 0.05$. (C) The numbers of perturbed genes in each group were presented as a Venn diagram.



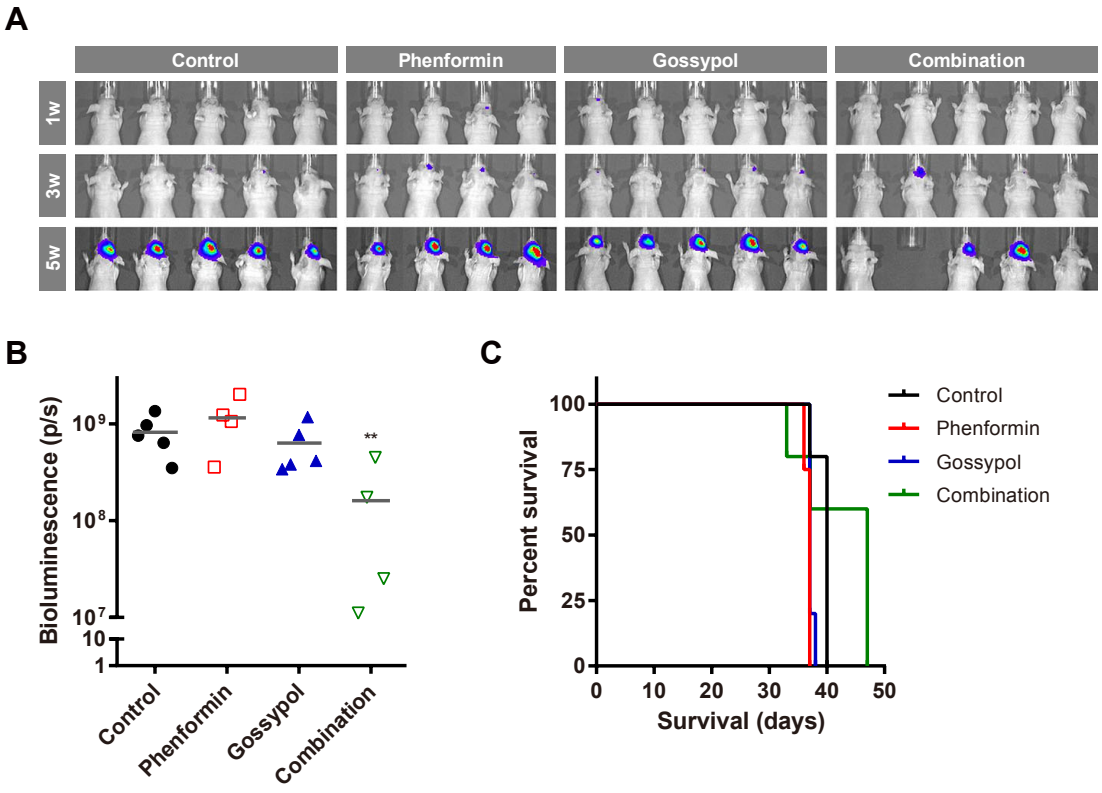
Supplementary Fig. S3. Evaluation of protein levels by flow cytometry.

After treatment with gossypol and phenformin for 72 h, PDPN and N-cadherin protein levels were measured by flow cytometry. (A) Only control and combination groups are indicated; the percentage of positive cells based on the right gating bar are indicated. (B) All groups are displayed.



Supplementary Fig. S4. ATP levels after malate treatment.

U87 spheres were treated with two different concentrations (5 and 10 mM) of malate for 12, 24, and 48 h, and then ATP levels were measured.



Supplementary Fig. S5. Therapeutic responses in a mouse orthotopic xenograft model.

In vivo effects of combined gossypol and phenformin treatment were tested in a mouse orthotopic xenograft model prepared using GSC11-luc cells. (A, B) Tumor volume was measured by bioluminescence imaging. Signal intensity was quantified as the sum of all detected photon counts (total flux) from tissues, presented as photon/s. Differences among groups were compared by one-way ANOVA with Tukey's *post hoc* test for multiple comparisons (**$P < 0.01$). (C) Survival probability for each group was estimated based on Kaplan-Meier curves. Log-rank test was performed to calculate statistical significance ($P < 0.05$).