## Supplementary figure legends

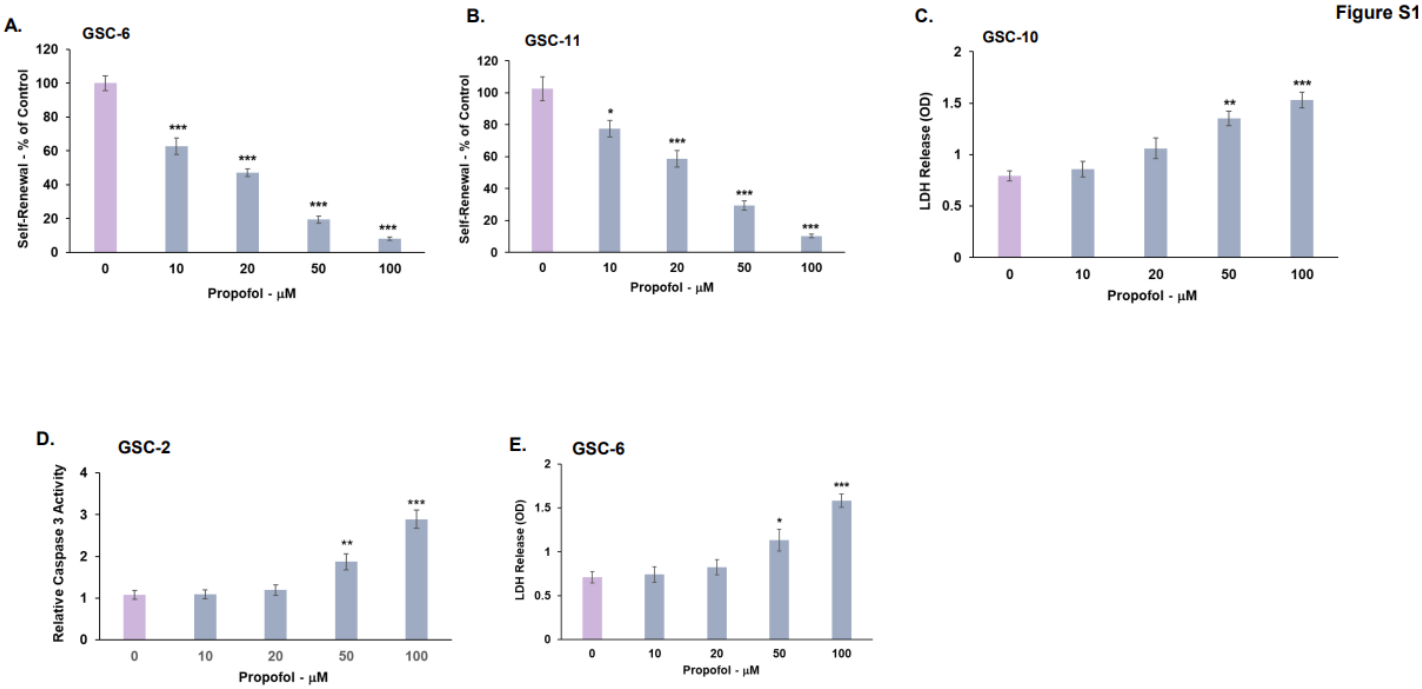



**Figure S1. Propofol effects on GSCs self-renewal and cell death**. GSC-6 (A) and GSC-11 (B) were plated at 100 cells/well in 96-well plates and treated with different propofol concentrations. The number of neurospheres per well was quantified after 14 days and presented as % of normalized control (A,B). Cell death was analyzed in GSC-10 (C) and GSC-2 (E) using LDH assay. Cell death is presented as relative average OD units. Cell apoptosis of propofol-treated GSC-2 was analyzed using caspase 3 activity (D). The results are presented as the means ± SD of three separate experiments. *P<0.05, **P<0.01, ***P<0.001. Significance was determined by two-tailed unpaired Student's t-test.

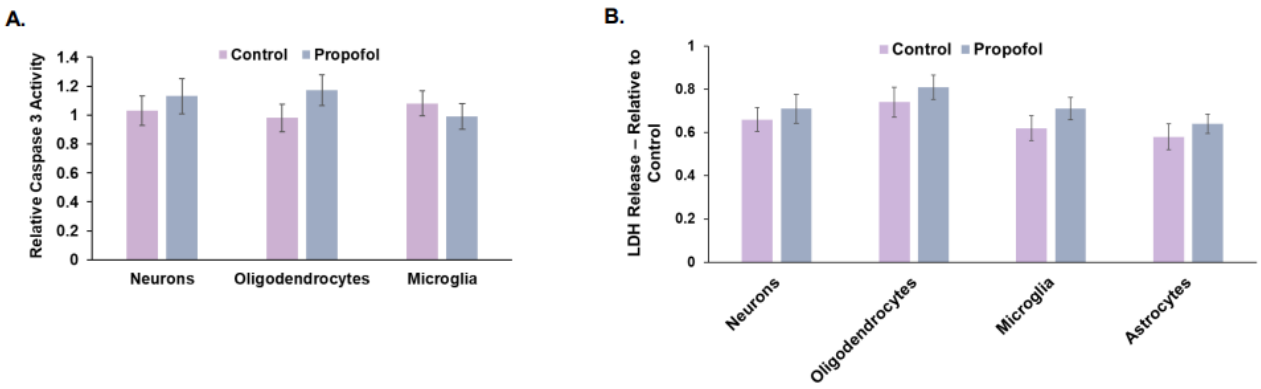



**Figure S2. Propofol does not exert cell death in human neural cells.** Human neurons, oligodendrocytes and microglia were cultured with 100 μM propofol for 48 hr and cell apoptosis was analyzed using caspase 3 activity (A). Cell death of human neurons, oligodendrocytes, microglia and astrocytes was analyzed by LDH assay (B). The results are presented as the means ± SD of three separate experiments. Significance was determined by two-tailed unpaired Student's t-test.

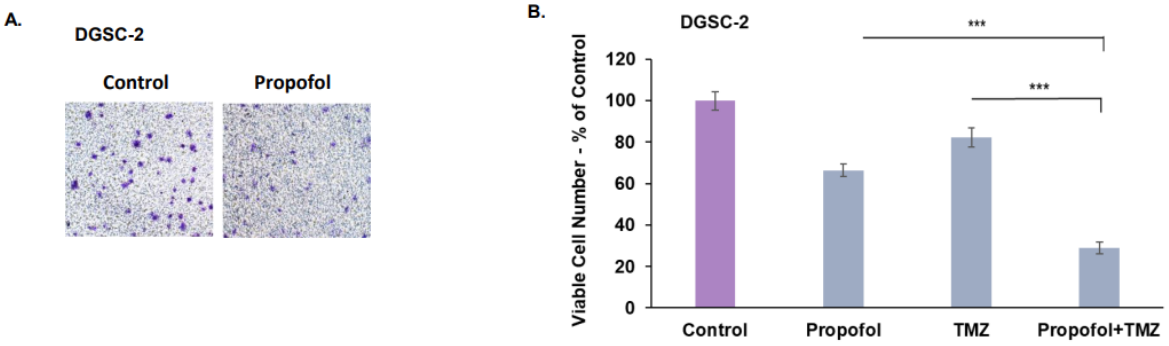



**Figure S3. Propofol inhibits migration and enhances the response of DGSC-2 to TMZ**. GSC-2 were differentiated in medium consisting of DMEM+10% FCS for a week. DGSC-2 were treated with propofol (20 μM) and cell migration was analyzed using transwell plates with 8 μm filter (A).

DGSC-2 were treated with propofol alone (10 μM) or with TMZ (25 μM). Cells proliferation was determined by determining cell number via trypan blue exclusion assay (B). Interaction analysis demonstrated a statistically significant interaction between propofol and TMZ that generated a synergistic inhibitory effect on cell proliferation, $F(1, 12) = 39.452$, $p < 0.0005$). The results represent as the means ± SD of four different experiments. ***P<0.001. Significance was determined by two-tailed unpaired Student's t-test.

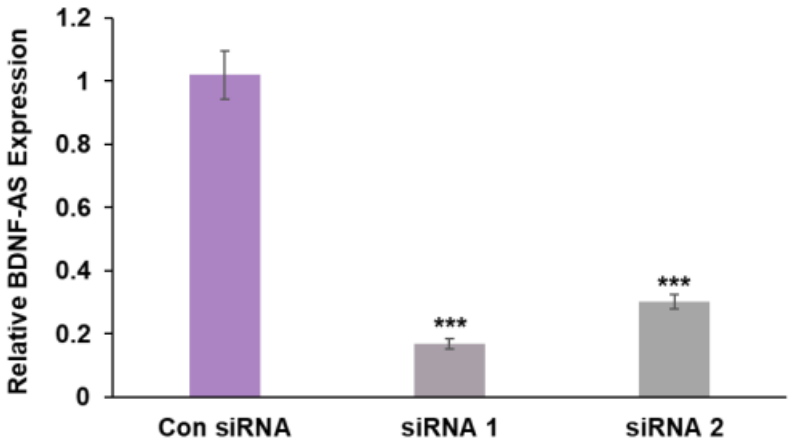



**Figure S4. Silencing of BDNF-As in GSCs.** GSC-10 were transfected with a control and two BDNF-AS siRNAs using siMPORTER reagent. The expression of BDNF-AS was determined after 48 hr using RT-PCR. The results represent mean values ± SD of three different experiments. ***P<0.001. Significance was determined by two-tailed unpaired Student's t-test.

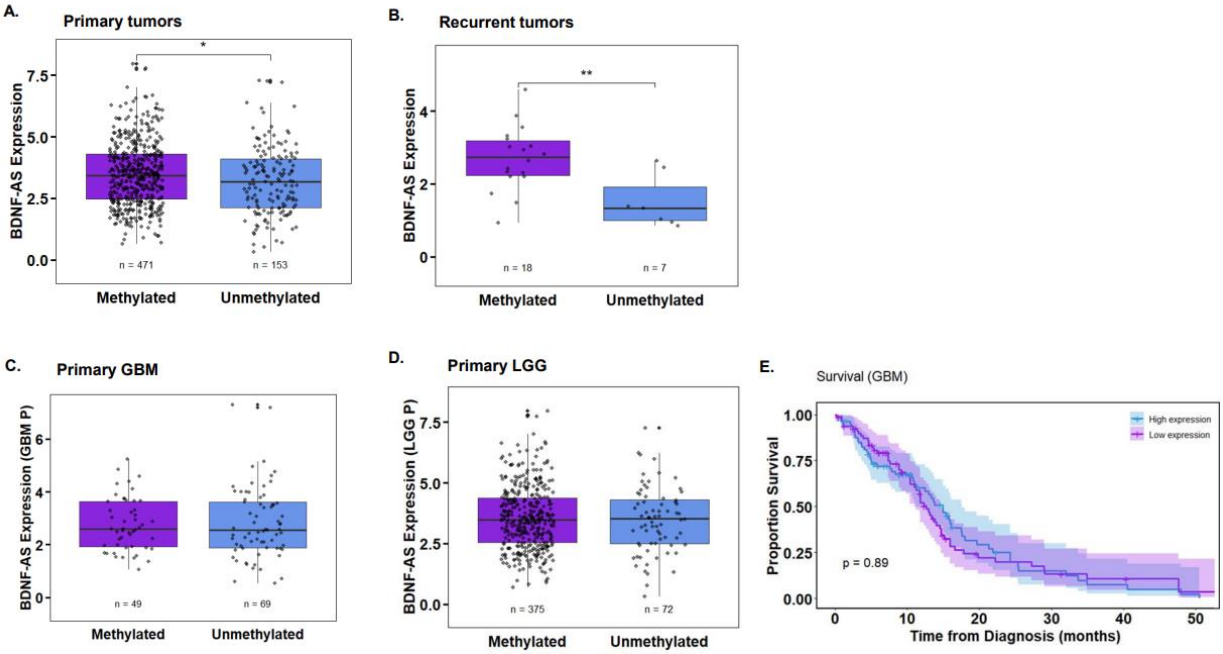
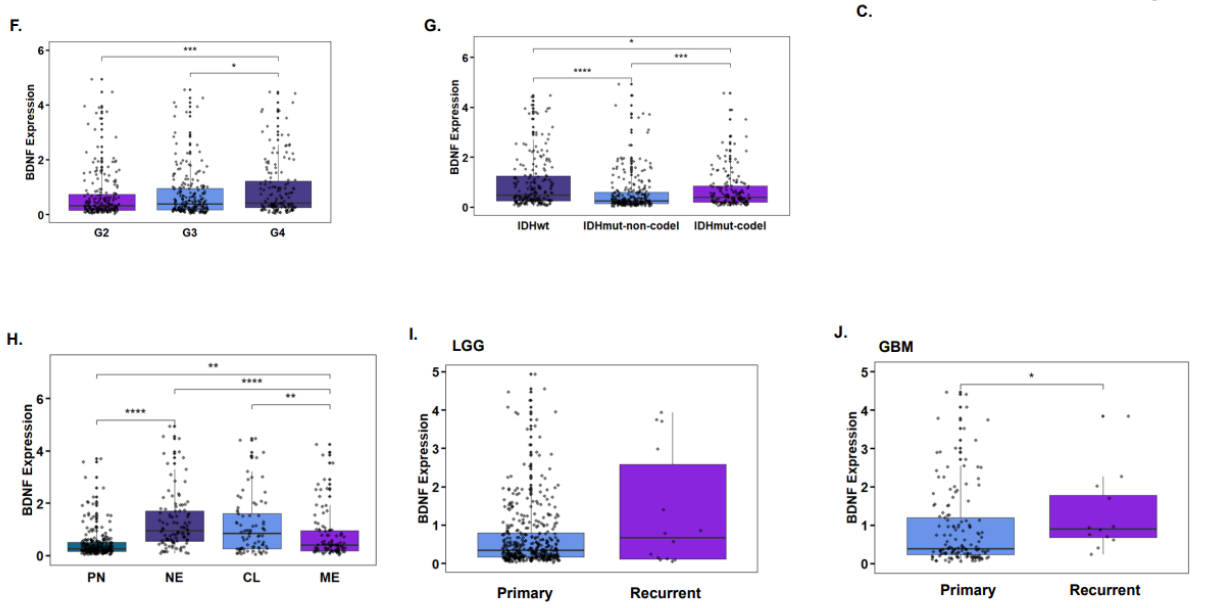

A.
Primary tumors
BDNF-AS Expression
n = 471
n = 153
Methylated
Unmethylated
B.
Recurrent tumors
BDNF-AS Expression
n = 18
n = 7
Methylated
Unmethylated
C.
Primary GBM
BDNF-AS Expression (GBM P)
n = 49
n = 69
Methylated
Unmethylated
D.
Primary LGG
BDNF-AS Expression (LGG P)
n = 375
n = 72
Methylated
Unmethylated
E.
Survival (GBM)
High expression
Low expression
Proportion Survival
p = 0.89
Time from Diagnosis (months)

Figure S5


F.
BDNF Expression
G2
G3
G4
G.
BDNF Expression
IDHwt
IDHmut-non-codel
IDHmut-codel
C.
H.
BDNF Expression
PN
NE
CL
ME
I.
LGG
BDNF Expression
Primary
Recurrent
J.
GBM
BDNF Expression
Primary
Recurrent

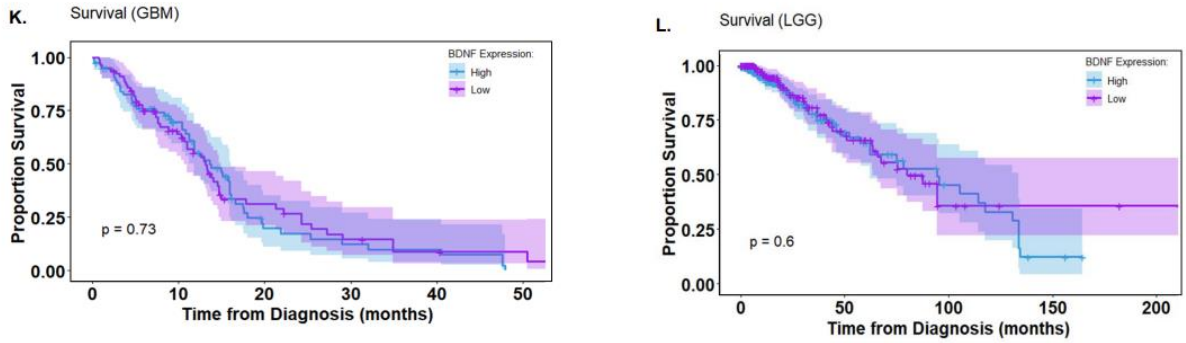



**Figure S5. Expression of BDNF in glial tumors.** The expression of BDNF-AS was analyzed in primary (A) and recurrent (B) glioma (GBM+LGG) and in primary GBM (C) and LGG (D) MGMT methylated and unmethylated tumors. Kaplan-Meier estimates of overall survival are plotted for GBM patients according to BDNF-AS expression, log-rank P = 0.89 (E). Relative expression of BDNF in LGG (G2, n=214; G3. N=225) and GBM (G4, n=158) was determined according to The Cancer Genome Atlas (TCGA data portal, Wilcoxon t-test P<0.0001) (F). BDNF expression was also determined in glioma tumors (GBM and LGG) by IDH status (IDH WT, n=217; IDHmut-codel n=256; IDHmut-non-codel, n= 167, Wilcoxon t-test P<0.0001) (G), and molecular subtypes (PN, n=242; NE, n=100; CL, n=80; ME, n=90, Wilcoxon t-test P<0.001) (H). The expression of BDNF in primary (n=144) and recurrent (n-12) LGG tumors, P<0.0001 (I) and primary (n=425) and recurrent (n-14) GBM tumors (J) was also analyzed.

Kaplan-Meier estimates of overall survival are plotted for GBM patients according to BDNF expression, log-rank P = 0.73, (K) and LGG patients according to BDNF expression, log-rank P = 0.89 (L).

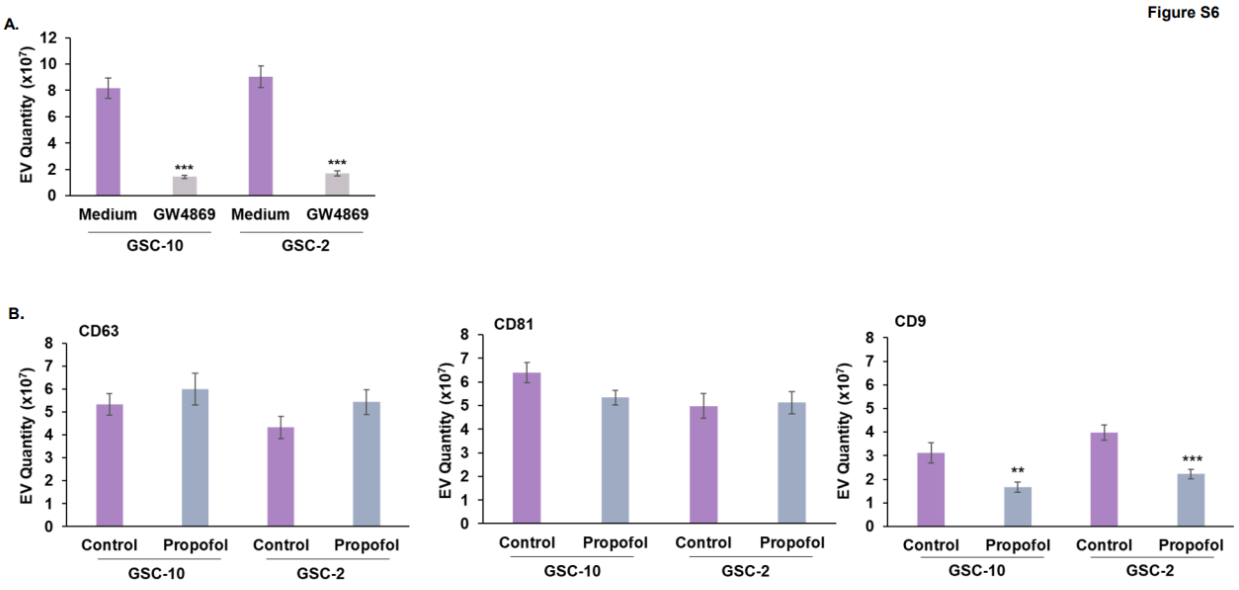



**Figure S6. Propofol effects on extracellular vesicle (EVs) secretion**. The effect of GW4869 (20 μM) on EV secretion was analyzed in both GSC-10 and GSC-2 after 20 hr of treatment (A). GSC-10 and GSC-2 were treated with propofol 20 μM for 24 hr. EVs were isolated using ExoQuick-TC Ultra kit and were analyzed for the relative expression of CD63, CD81 and CD9 using ELISA (B). The results represent mean values ± SD of three different experiments. **P<0.01, ***P<0.001. Significance was determined by two-tailed unpaired Student's t-test.

**Supplementary Table 1. De-identified patient information of GSCs**

| Cell Line | Age@diagnosis (years) | Gender | OS (days) | MGMT | P53 mutation status | Mesenchymal markers | IDH status |
|---|---|---|---|---|---|---|---|
| **GSC-10** | 39 | F | 717 | M | wt | L | WT |
| **GSC-2** | 54 | M | 432 | M | wt | H | WT |
| **GSC-6** | 54 | F | 339 | U | R175H | H | WT |
| **GSC-11** | 45 | M | 646 | U | M133T | L | WT |

For each GSC, the age, gender, survival data, MGMT (U-unmethylated and M-methylated), IDH and p53 status are presented. Mesenchymal phenotypes of the GSCs were determined by the relative expression of YKL40, SMA and GTGF.

**Table S2**

**Sequences of primers used for RT-PCR**

| | | |
|---|---|---|
| **BDNF** | **F:** GACAAGGCAACTTGGCCTAC | **R:** CGTGTTCGAAAGTGTCAGCC |
| **BDNF-AS** | **F**: CCGTGAGAAGATCTCATTGGG | **R**: CGTGCTCAAAAGTGTCAGCC |
| **TGF-β1** | **F**: CAAGCAGAGTACACACAGCAT | **R**: TGCTCCACTTTTAACTTGAGCC |
| **CD44** | **F:** CTCCACCTGAAGAAGATTGT | **R:** AAGATGTAACCTCCTGAAGT |
| **Vimentin** | **F:** GCAAAGATTCCACTTTGCGT | **R:** GAAATTGCAGGAGGAGATGC |
| **OCT4** | **F:** ATCAGCCACATCGCCCAGCA | **R**: CCCAGCAGCCTCAAAATCCT |
| **Nanog** | **F:** ACCTATGCCTGTGATTTGTGG | **R**: GTTGTTTGCCTTTGGGACTG |
| **SOX2** | **F:** CCAGAAAAACAGCCCGGACC | **R**: CGCTTCTCCGTCTCCGACAA |
| **YKL40** | **F:** TGCCCTTGACCGCTTCCTCT | **R**: TTGATGAAAGTCCGGCGACT |
| **CTGF** | **F:** GTGTGCACCGCCAAAGATG | **R**: CAACCACGGTTTGGTCCTTG |
| **Twist1** | **F:**TAGAAGTCTGAACACTCGTT | **R**: AATTCCTCTGATTGTTACCATT |
| **IL-10** | **F**:TCTCCGAGATGCCTTCAGCAGA | **R**: TCAGACAAGGCTTGGCAACCCA |
| **CD86** | **F**: AGCCTTATCGGAAATGATCCAG | **R**: GGCCTTGTAGACACCTTGGT |
| **CD206** | **F**: CATCAGGGTGCAAGGAAGG | **R**: GTCCAGGCACTGAAAGTGGA |
| **S12** | **F**:TGCTGGAGGTGTAATGGACG | **R**: CAAGCACACAAAGATGGGCT |
| **β2MG** | **F:**TAAGTGGGATCGAGACATGTAAGC | **R**: CTAGAGCTACCTGTGGAGCA |