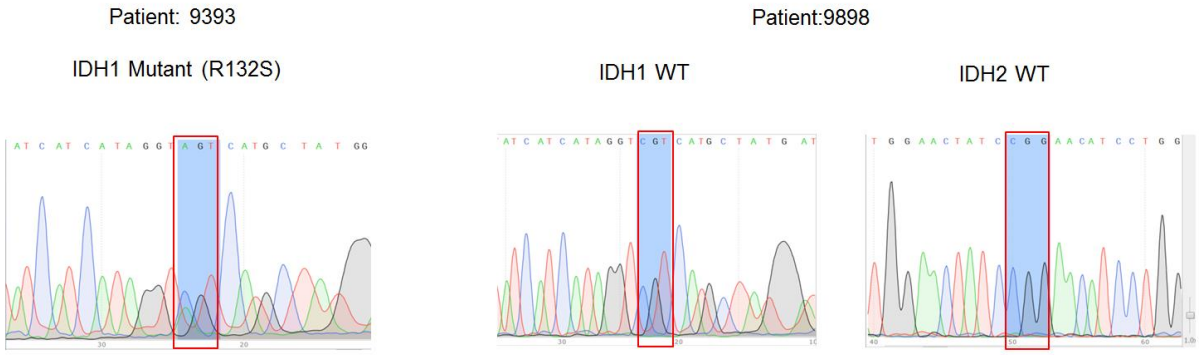
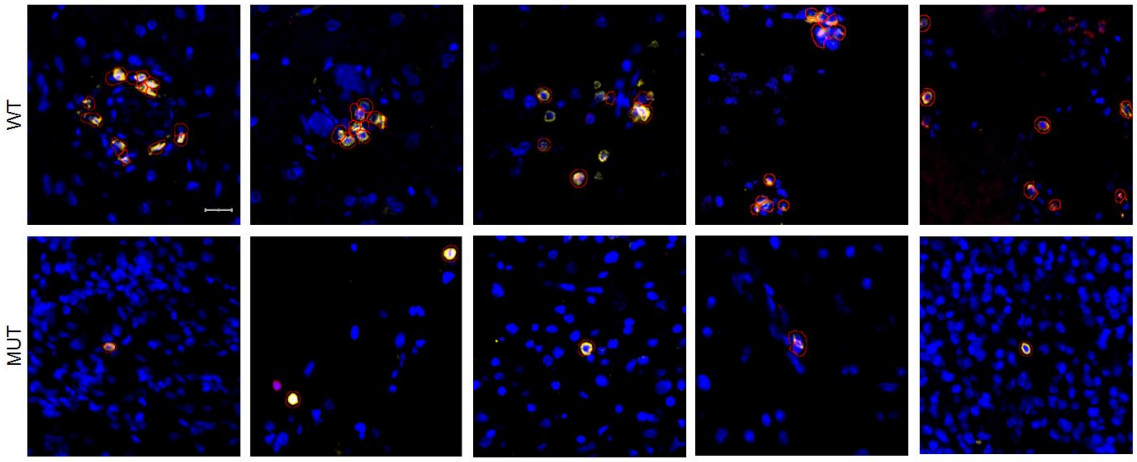
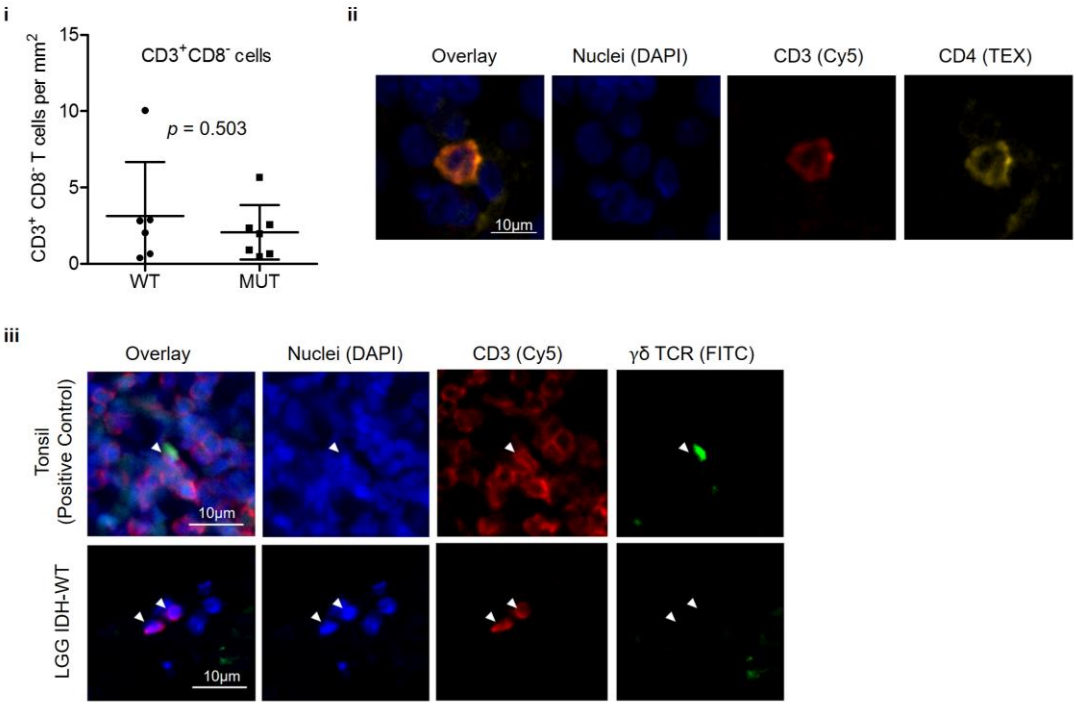
Supplementary Materials:



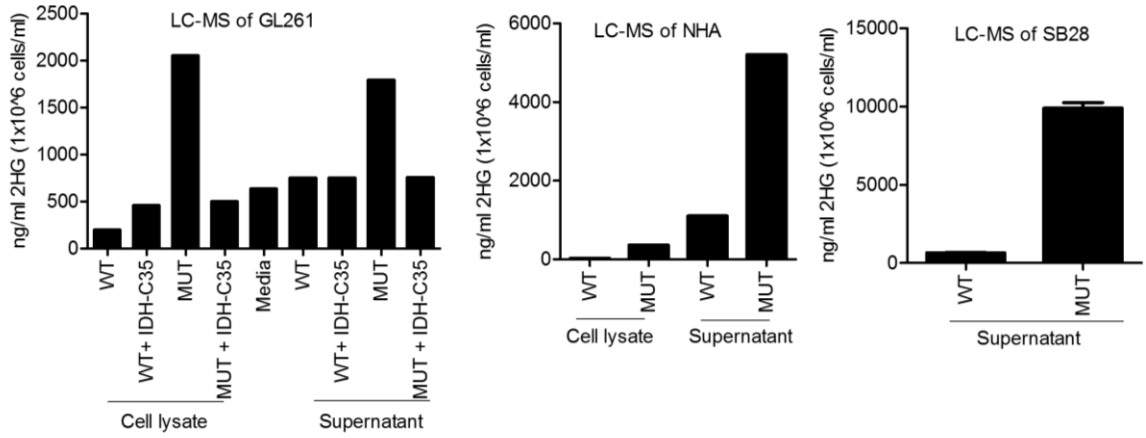
Supplementary Figure 1. IDH1 and IDH2 mutation site sequences on WHO grade III patient samples. Genomic DNA samples extracted from punch biopsies from either FFPE or frozen tumor blocks were subject to PCR amplification, followed by sequencing by Quintara Bio (San Francisco, CA). Data files were analyzed by using SnapGene Viewer. Shown are representative DNA sequences from Patient 9393 with the R132S mutation in IDH1 and Patient 9898 with both WT IDH1 and WT IDH2 genes. The red boxes indicate DNA coding for amino acids 132 and 172 for IDH1 and IDH2, respectively.



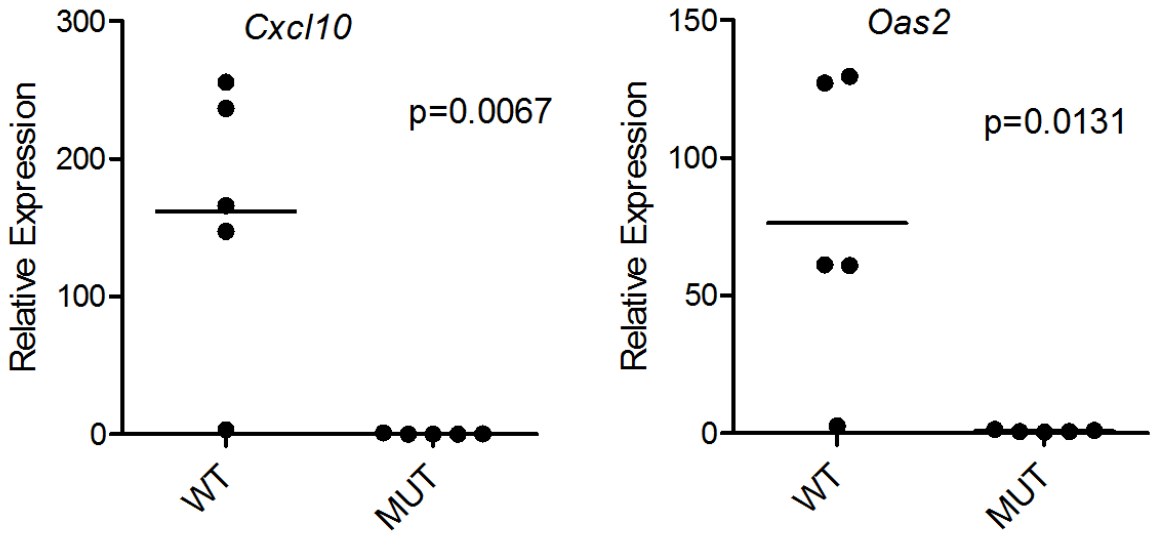
Supplementary Figure 2. $CD3^+CD8^+$ cells in WHO grade III glioma tissue by immunofluorescence. Merged immunofluorescence staining of CD3 (red), CD8 (yellow) and nuclei (blue) on FFPE tumor sections from WHO grade III IDH-WT (n=5) and IDH-MUT (n=5) glioma cases. Each panel represents an individual case. Red circles represent automated cell masks on $CD3^+CD8^+$ double positive cells as determined by StrataQuest software. The middle panel of the MUT group also appears in the merged image for the representative MUT case in Figure 1A. Scale bar: 20 μm. Immunofluorescence microscopy was performed on a Zeiss Axio-Imager Z2 and X-Cite XLED1 High Power LED fluorescence source using a 20x/0.5 NA objective and Hamamatsu Orca-Flash 4.0 camera. Images were acquired with TissueFAXS software 4.2, and analyzed with StrataQuest software.



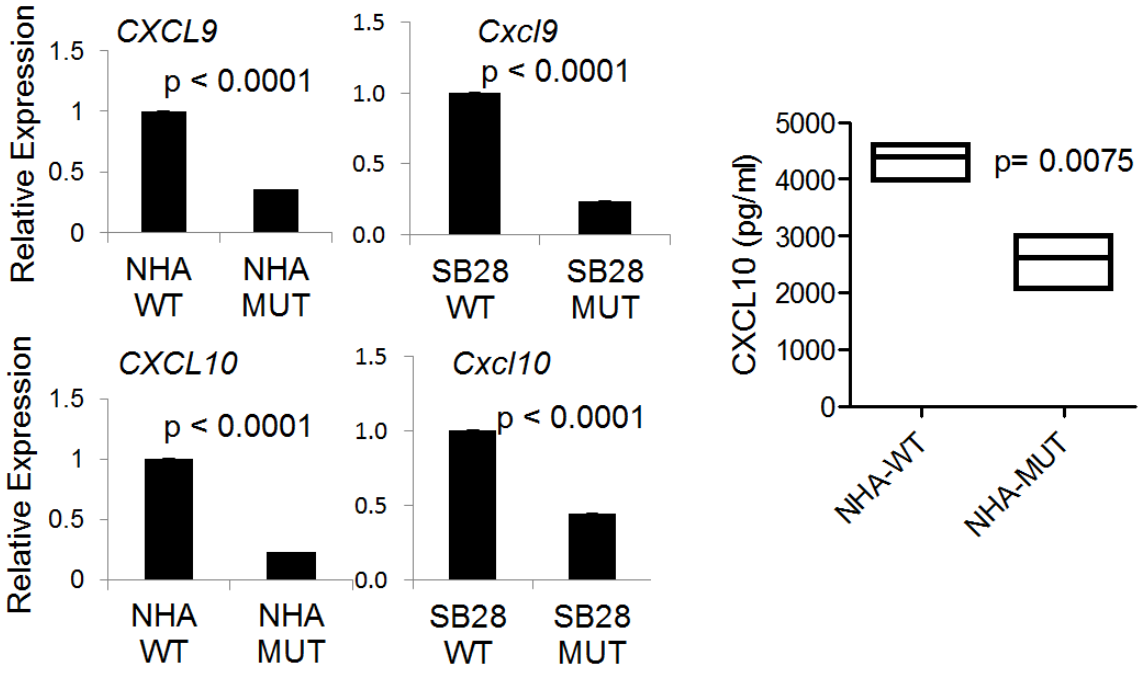
Supplementary Figure 3. $CD3^+CD8^-$ cells/mm^2 in WHO grade III gliomas. (i) Number of $CD3^+CD8^-$ cells per area (mm^2) of tumor, calculated for each IDH-WT (n=6) and IDH-MUT (n=7) case using StrataQuest software. Each dot represents a value from a single patient and black lines represent the mean of samples in a group. *P* value was determined by a 2-sided, unpaired t-test. **(ii)** Representative staining showing the presence of a $CD3^+CD4^+$ T-cell in a Grade III glioma sample. **(iii)** Positive control staining of a γδ TCR (Green) on a $CD3^+$ T-cell (Red) in a tonsil section. Representative staining demonstrating absence of γδ staining on T-cells from evaluated IDH-WT (n=5 cases) and IDH-MUT (n=5 cases) grade III glioma sections.



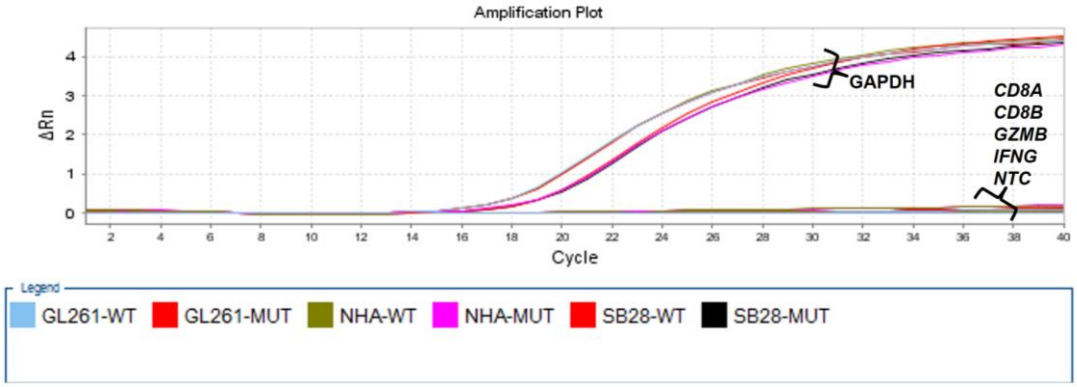
Supplementary Figure 4. 2HG levels in GL261, NHA and SB28 models by LC-MS. Aliquots of $1x10^6$ $GL261^{R132H}$, NHA^{R132H}, and $SB28^{R132H}$ cells were cultured for 24 hours with fresh media. Supernatant was collected and cells were re-suspended in 80% methanol and 20% deionized water for analysis. Samples were analyzed for 2HG on a Sciex API-5000 LC-MS/MS system. **(Left panel)** 2HG levels detected in GL261-WT or GL261-MUT lysate or supernatant with or without IDH-C35 (1 μM for 3 days). **(Middle panel**) 2HG levels in cell lysates or supernatant from NHA-WT or NHA-MUT cells. (**Right panel**) 2HG levels in supernatant from cultured SB28-WT or SB28-MUT cells.



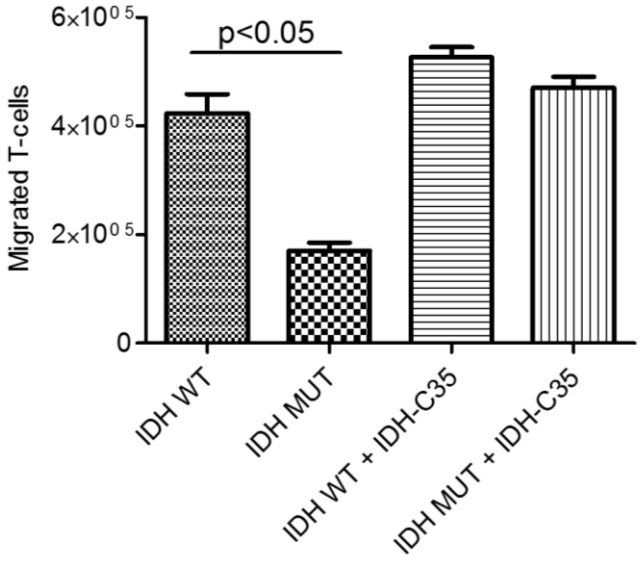
Supplementary Figure 5. IFN-γ-inducible and chemokine-related genes in GL261^{WT} and GL261^{R132H} tumors. C57BL/6 mice received intracranial injections of 1x10^5 GL261^{WT} (WT) or GL261^{R132H} (MUT) glioma cells. Day 21 tumors were removed from mice and further assessed by RT-PCR for expression of *Cxcl10* and *Oas2*. *P* values were determined by 2-tailed, unpaired t test.



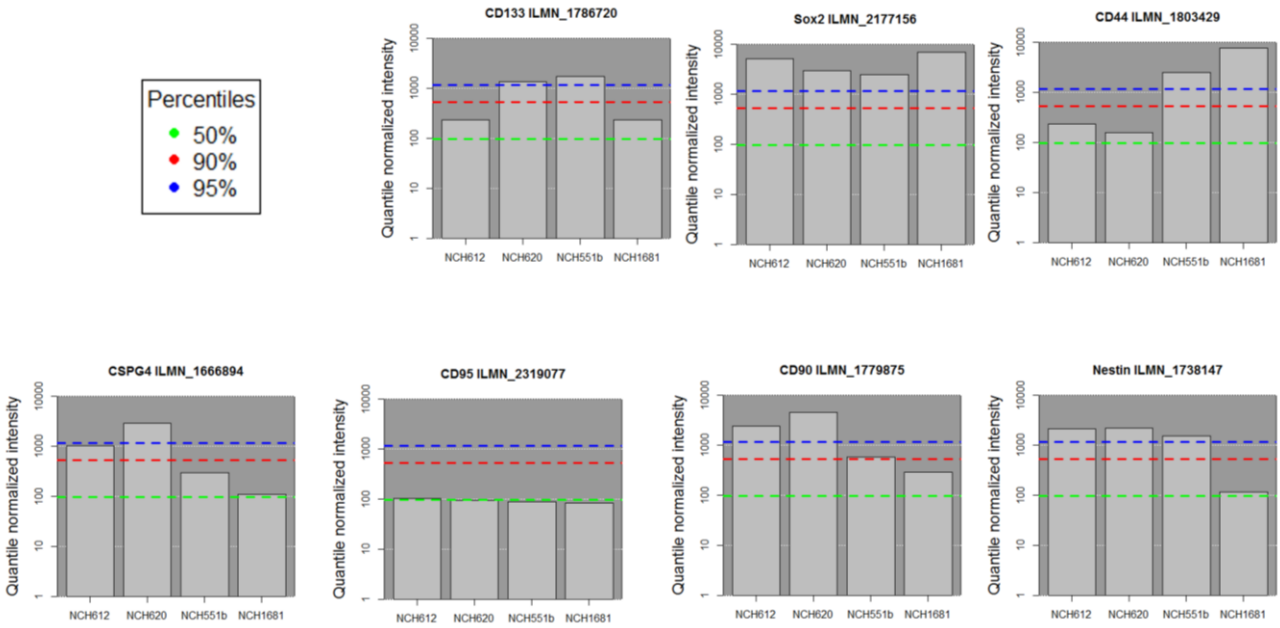
Supplementary Figure 6. CXCL9 and CXCL10 levels in NHA^{WT}/NHA^{R132H} and SB28^{WT}/SB28^{R132H} cells. (Left) RT-PCR analysis of *CXCL9* and *CXCL10* on RNA derived from NHA^{R132H} (NHA-MUT), SB28^{R132H} (SB28-MUT) NHA^{WT} (NHA-WT) and SB28^{WT} (SB28-WT) cells. RNA levels were normalized to *Gapdh* and are shown relative to WT samples. **(Right)** CXCL10 ELISA performed on supernatant from NHA-WT and NHA-MUT cells stimulated with IFN-γ for 12 hours. Results shown are representative of at least 2 independent experiments. *P* values were determined by 2-tailed, unpaired t test.



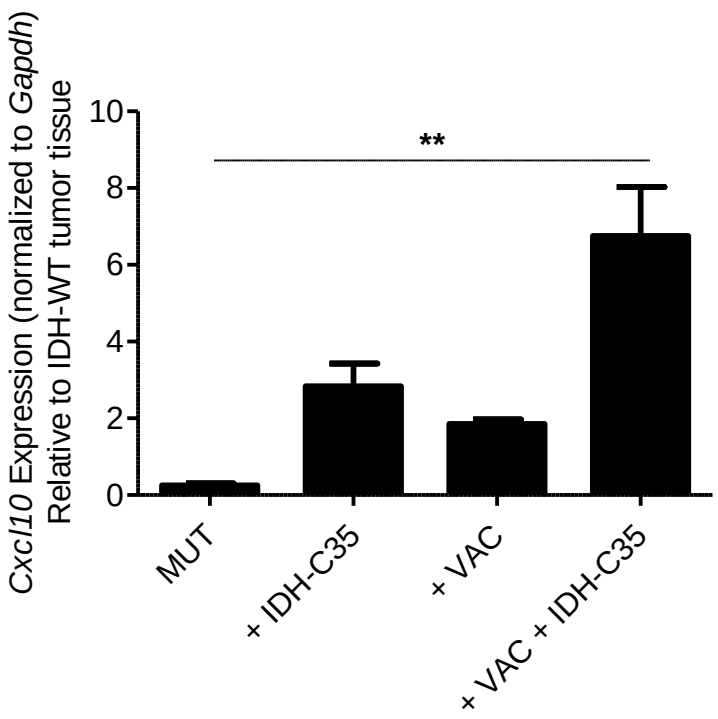
Supplementary Figure 7. Expression levels of immune-related genes in IDH-WT and IDH-MUT cell lines. Amplification plots from RT-PCR analysis of *GAPDH*, *CD8A*, *CD8B*, *GZMB*, and *IFNG* in total RNA derived from NHA^{R132H} (NHA-MUT), $SB28^{R132H}$ (SB28-MUT) NHA^{WT} (NHA-WT), $SB28^{WT}$ (SB28-WT), $GL261^{R132H}$ (GL261-MUT), and $GL261^{WT}$ (WT) cells. RNA levels were normalized to *GAPDH*. NTC indicated no transcript control.



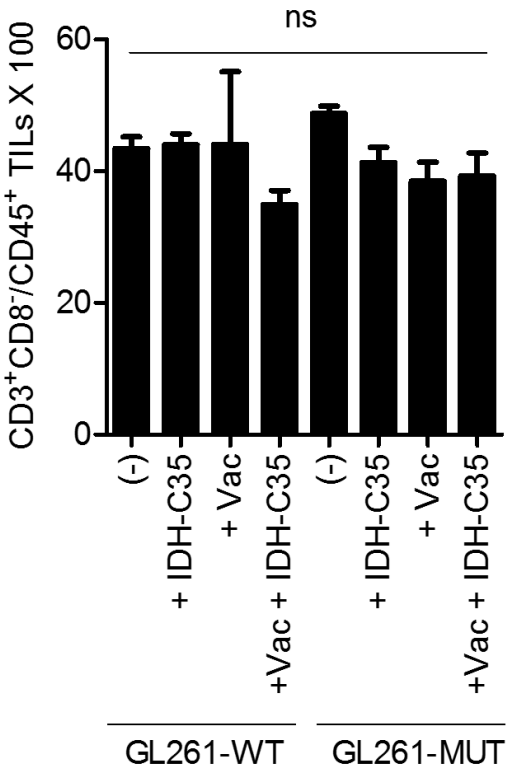
Supplementary Figure 8. Transwell migration of CD8^{+} T-cells towards SB28^{WT}/SB28^{R132H} CM. Chemotaxis of 1x10^{6} CD8^{+} T-cells pre-stimulated for 48 hours with anti-CD3/anti-CD28 towards SB28^{WT} (IDH-WT) SB28^{R132H} (IDH-MUT) glioma cell CM generated in the absence or presence of IDH-C35. CM was diluted 1:1 with fresh media. Migrated cells were counted after 12 hours using a Countess^{TM} automated cell counter. Results shown are representative of 2 independent experiments. *P* values were determined by 2-tailed, unpaired t test.



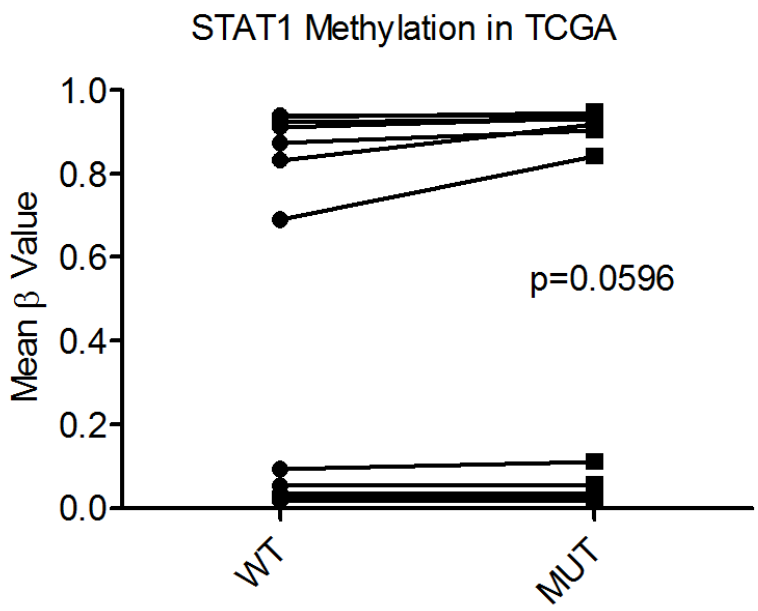
Supplementary Figure 9. Normalized expression levels of glioma stem cell-related genes in WHO grade III glioma-derived neurospheres. Expression levels of cancer stem cell-related genes in NCH612, NCH620, NCH551b, and NCH1681 cell lines based on microarray analyses. Data were normalized across all genes in each data set. Colored lines indicate the 50% percentile (considered as low or no expression) and the 90 and 95% percentile (highly expressed genes high expressed) probes (stated in the title). ILMN numbers adjacent to gene names indicate the unique probe evaluated for each gene.



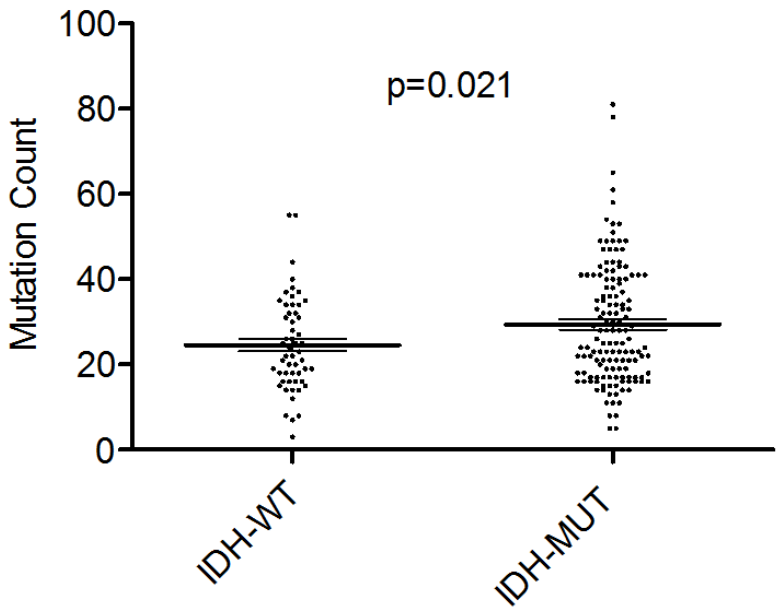
Supplementary Figure 10 Combination therapy of GL261-MUT tumor bearing mice with GAA vaccine and IDH-C35 enhances *Cxcl10* expression. RT-PCR analysis of tumor tissue from day 21 treated GL261-MUT tumor-bearing mice. Mice were treated with mock vaccine and vehicle (MUT; n=2), mock vaccine and IDH-C35 (+IDH-C35; n=3), GAA vaccine and vehicle (+VAC; n=2), or GAA vaccine + IDH-C35 (VAC + IDH-C35; n=3). One way ANOVA analysis was performed with a Dunnett multiple correction test. ***P<0.01*



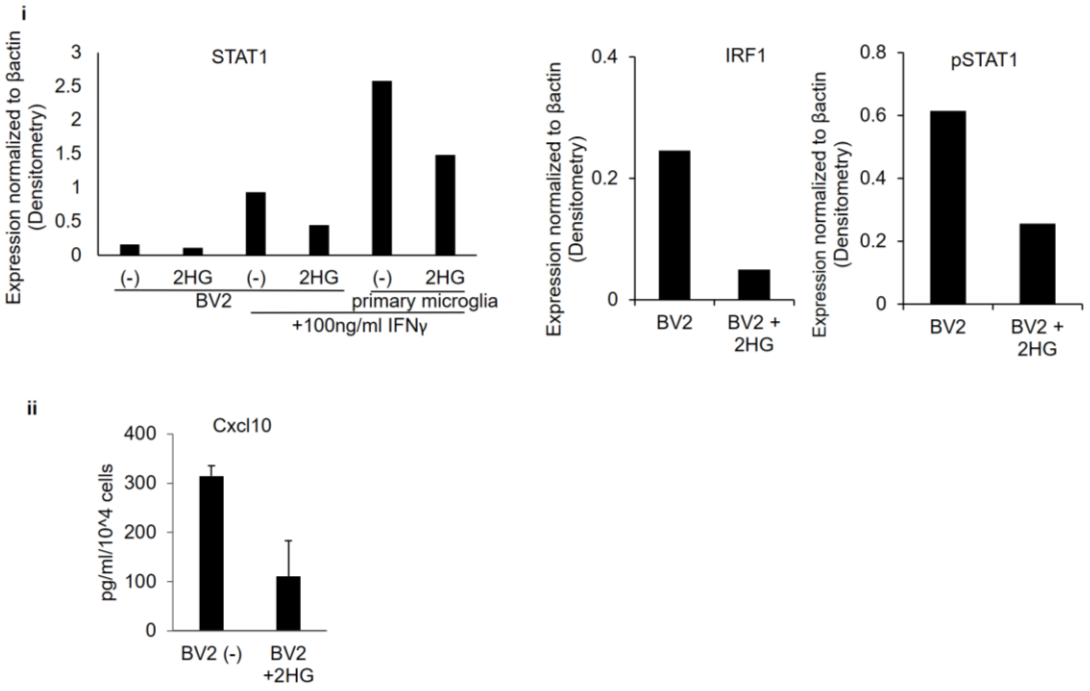
Supplementary Figure 11. No difference in $CD3^+CD8^-$ T-cells between GL261-WT and GL261-MUT mice between treatment groups. Flow cytometric analyses of tumor-infiltrating $CD3^+CD8^-$ cells as a percentage of total $CD45^+$ cells. Analyzed cells were gated on live lymphocytes. One way ANOVA with Dunnet's multiple correction test was performed. No significant differences were observed in any condition. ns=*P>0.05*



Supplementary Figure 12. Methylation of STAT1 promoter CpG sites in IDH-WT and IDH-MUT TCGA cases. 450k Methylation data from LGG patients were downloaded from the TCGA (tcga-data.nci.nih.gov). Mean β values from TCGA IDH-WT (WT; n=58) and IDH-MUT (MUT; n=149) cases. Each bar represents the mean β values from a single CpG methylation site in the STAT1 promotor compared between IDH-WT and IDH-MUT cases. *P* values were determined by 2-tailed, paired t test.



Supplementary Figure 13. Mutation counts in in IDH-WT and IDH-MUT TCGA cases. Higher numbers of mutations in IDH-MUT TCGA cases compared with IDH-WT TCGA cases. Data were downloaded from the TCGA data portal (UCSC Automated Mutation Calling, Level 2, downloaded November 4, 2015) from which the number of mutations was counted per sample. Mutation counts were compared between IDH-WT and IDH-MUT cases. Each dot represents mutation counts from a single patient. Black bars and error bars represent mean values and standard deviations, respectively. *P* values were determined by 2-tailed, unpaired t test.



Supplementary Figure 14. STAT1 signaling and CXCL10 levels in 2HG-treated BV2 microglia cells. (i) Western blot was performed on protein lysates from BV2 microglia cells treated with 1 mM 2HG for 3 days with or without 10 ng/ml IFN-γ for 12 hours. STAT1, pSTAT1 and IRF1 levels were determined relative to β-actin by ImageJ software. **(ii)** CXCL10 protein expression levels in CM from IFN-γ-treated BV2 cells were assessed by Quantikine ELISA (*P=0.0093)*. Results shown are representative of 2 independent experiments. *P* values were determined by 2-tailed, unpaired t test.