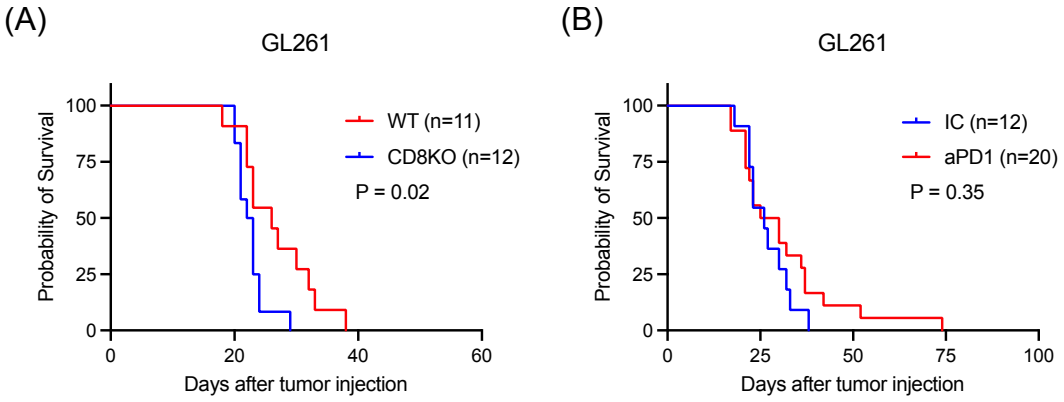
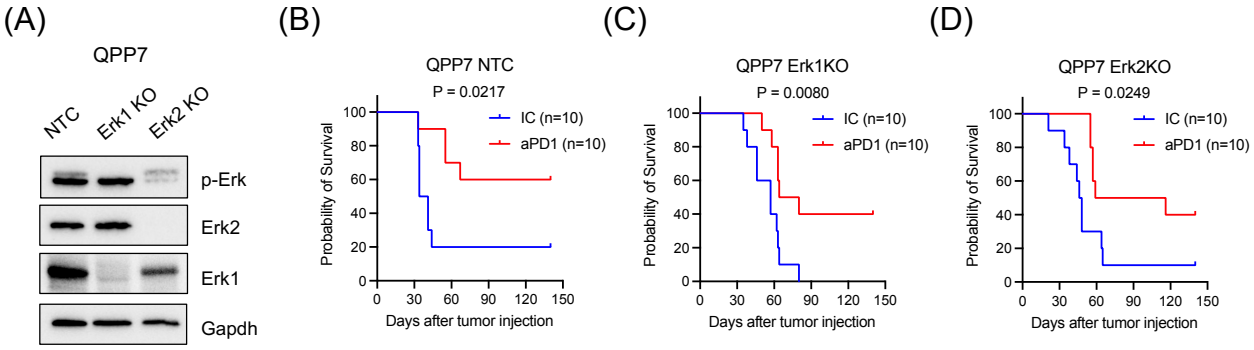
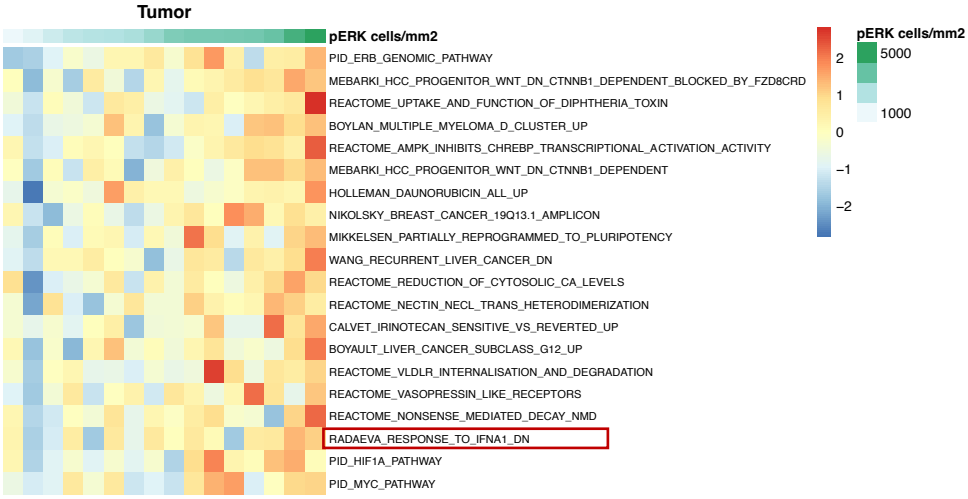


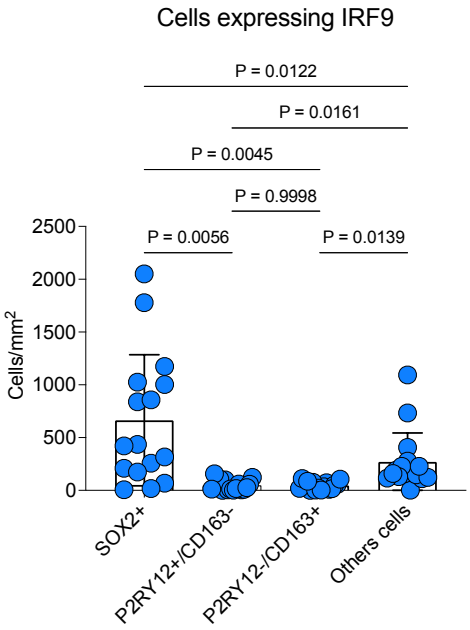
Supplementary Figure 1. (A) Kaplan-Meier survival curves from the kinome-wide CRISPR/Cas9 screen, comparing GL261-bearing C57BL/6 WT (n = 11) and *Cd8* KO mice (n = 12). (B) Kaplan-Meier survival curves from the kinome-wide CRISPR/Cas9 screen conducted in C57BL/6 WT mice comparing IC (n = 12) and aPD-1 (n = 20) treated groups. The P-values were calculated using the log-rank test.



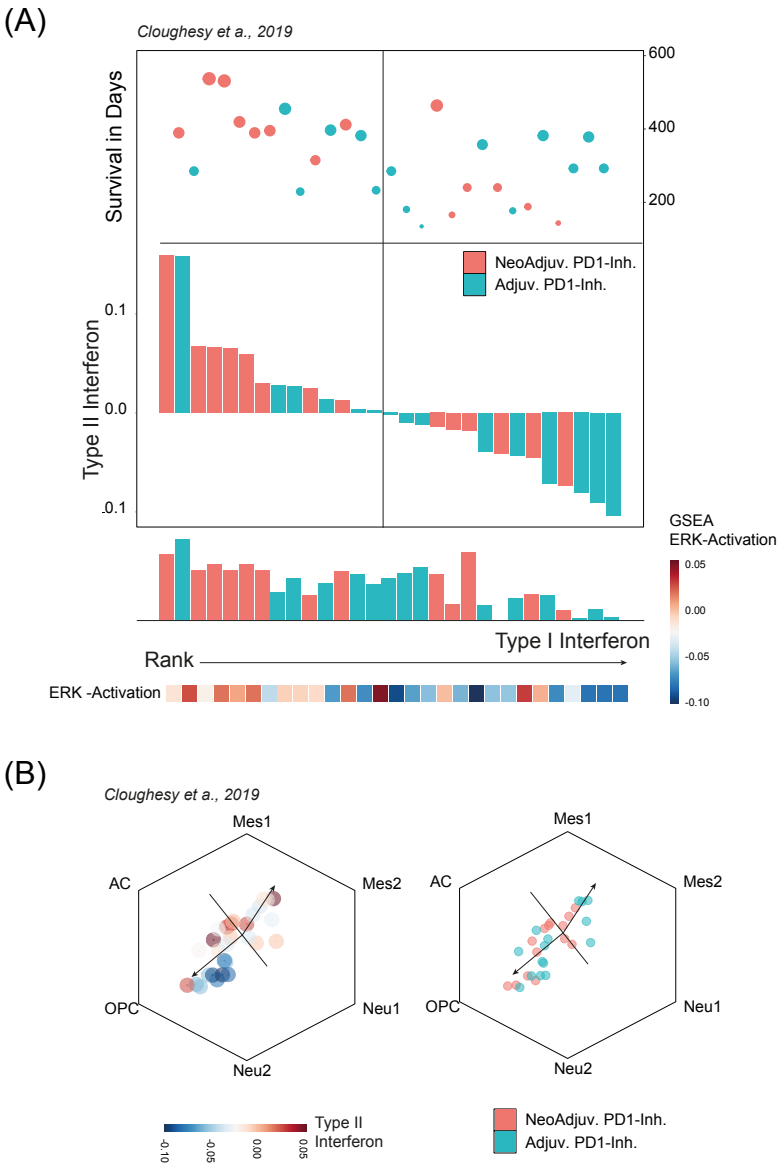
Supplementary Figure 2. (A) Western blot analysis showing KO of Erk1 or Erk2 in immunotherapy-sensitive QPP7 mouse glioma model. (B) Kaplan-Meier survival curves of QPP7-NTC bearing mice treated with IC (n = 10) or aPD-1 (n = 10). (C) Kaplan-Meier survival curves of QPP7-Erk1 KO bearing mice treated with IC (n = 10) or aPD-1 (n = 10). (D) Kaplan-Meier survival curves of QPP7-Erk2 KO bearing mice treated with IC (n = 10) or aPD-1 (n = 10). The P-values were calculated using the log-rank test.



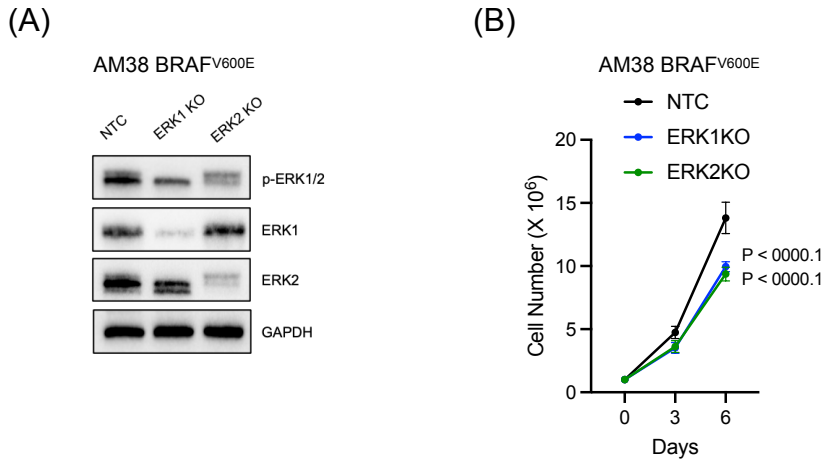
Supplementary Figure 3. Differential gene expression analysis of scRNA-seq data from human GB patient samples, categorized by continuous levels of p-ERK.



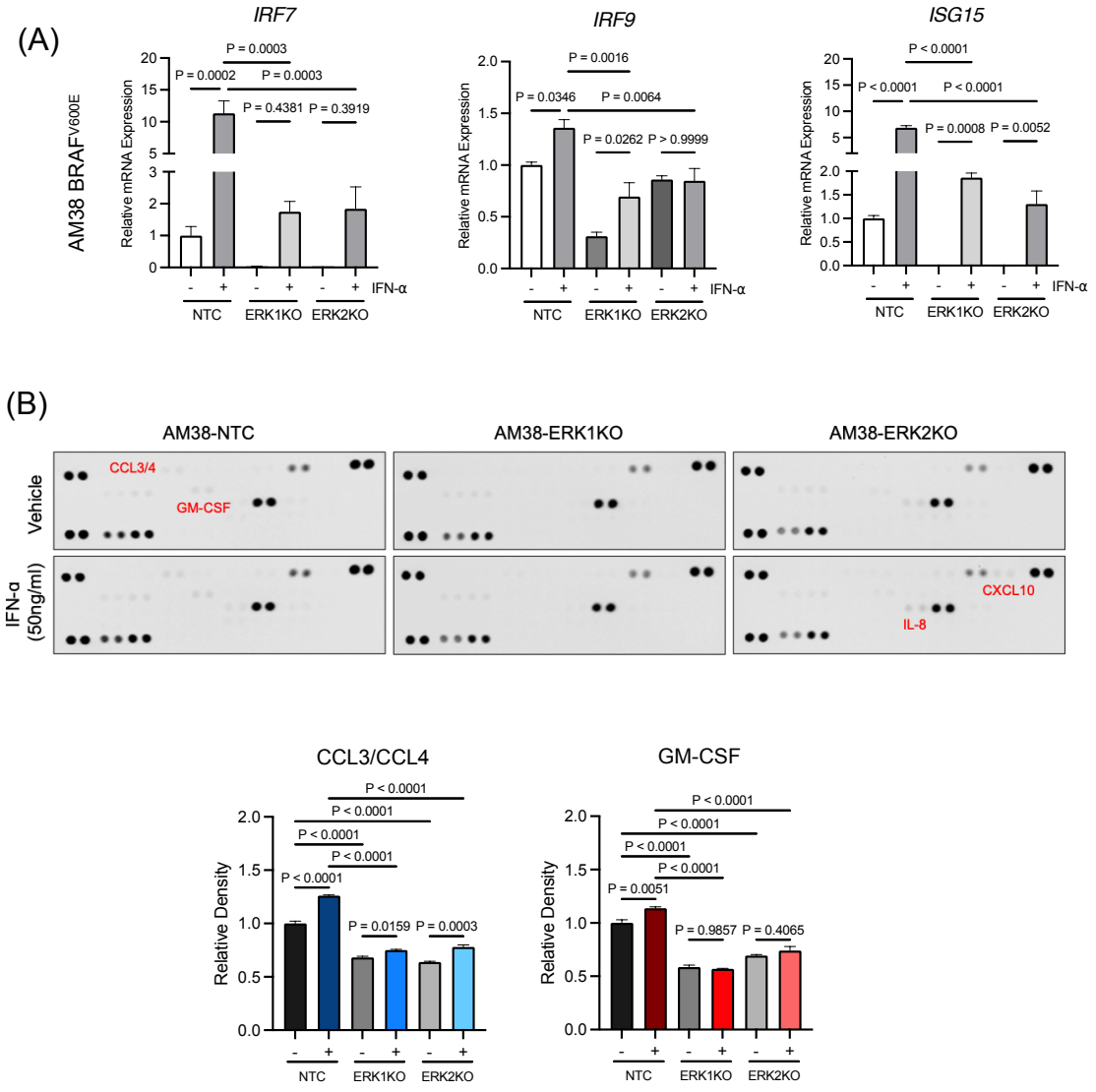
Supplementary Figure 4. Quantification analysis of immunofluorescence analysis staining for SOX2, P2RY12, CD163, IRF9, and DAPI in GB samples. One-way ANOVA was used to determine statistical significance, and corresponding P-values are shown in the figure.



Supplementary Figure 5. (A) Analysis derived from Cloughsey's 2019 study, showing overall expression levels of Type I IFN across all cohorts and their respective survival rates. (B) The left panel depicts cell types and Type I interferon signaling, while the right side compares adjuvant PD-1 inhibitor therapy with neoadjuvant PD-1 inhibitor therapy.

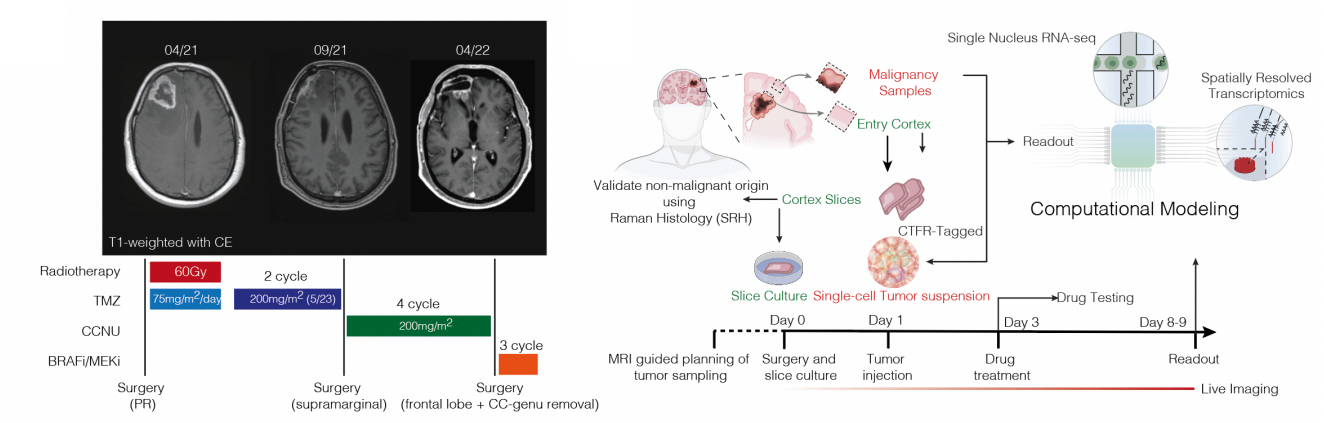


Supplementary Figure 6. Characterization of AM38-ERK KO cell lines. (A) Western blot analysis demonstrating the KO of ERK1 and ERK2 in the AM38 BRAF^{V600E} cell line. (B) Cell proliferation assay showing the total cell number count for both ERK1 and ERK2 KO cell lines over time. The graph represents the mean ± SD (n = 4), one-way ANOVA was used to determine statistical significance, and corresponding P-values are shown in the figure.

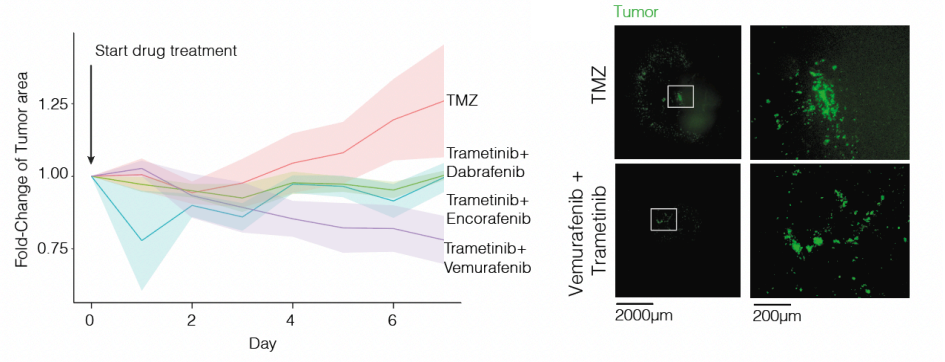


Supplementary Figure 7. (A) Quantitative RT-PCR results showing transcript levels of *IRF7*, *IRF9*, and *ISG15* in AM38-NTC, ERK1 KO, and ERK2 KO cells following exposure to IFN-α. Data are presented as mean ± SD (n = 4). (B) Cytokine secretion analysis using a human cytokine array kit (top panel). Bar graphs represent the relative fold change in CCL3/CCL4 (left) and GM-CSF (right) secretion from the culture supernatants of AM38-NTC, ERK1 KO, and ERK2 KO cells. Statistical significance was determined using one-way ANOVA, and P-values are indicated.

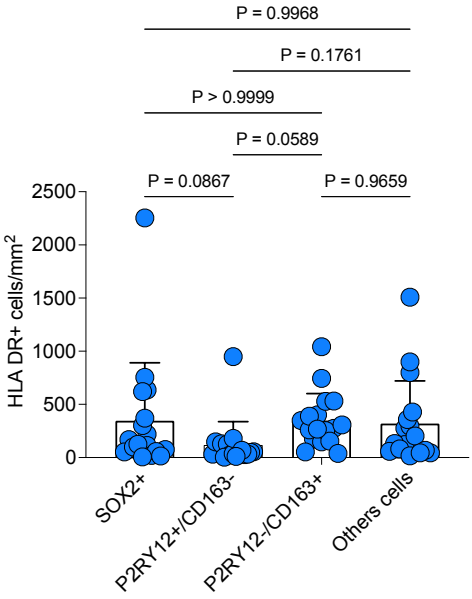
(A)



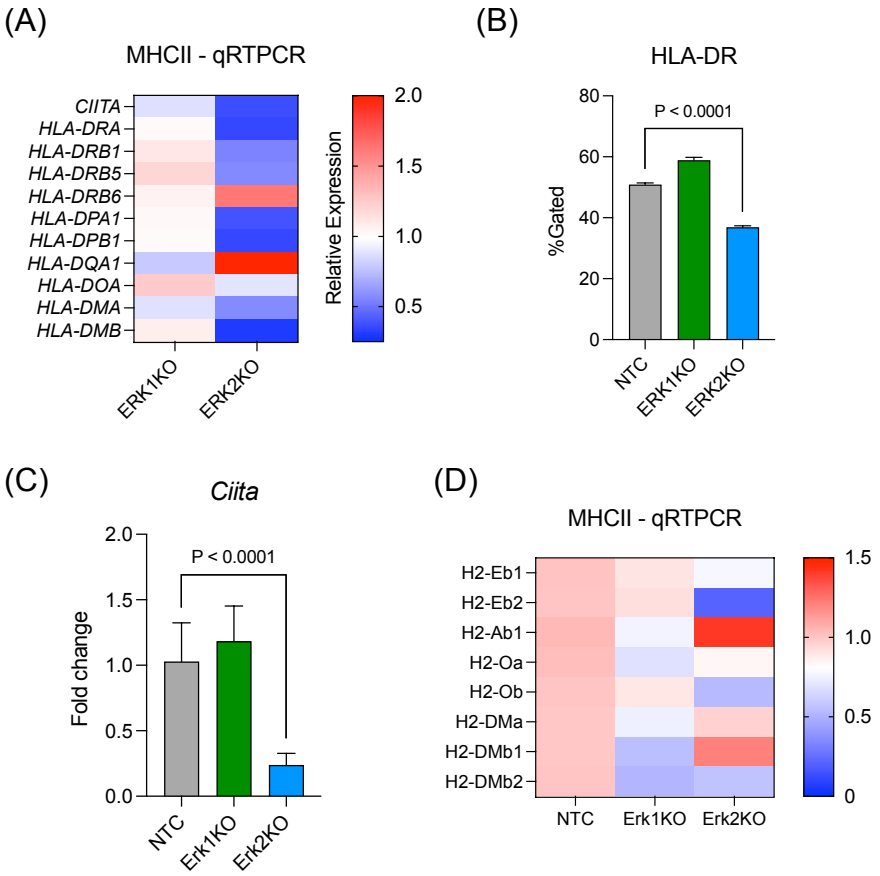
(B)



Supplementary Figure 8. (A) Brief illustration of autologous human neocortical slice model from BRAFV600E mutated GB patient. Tumor cells were implanted in cultivated cortex slices, then treated with temozolomide or BRAFi/MEKi combination.



Supplementary Figure 9. Quantification analysis of immunofluorescence analysis staining for SOX2, P2RY12, CD163, HLA-DR, and DAPI in GB samples. One-way ANOVA was used to determine statistical significance, and corresponding P-values are shown in the figure.



Supplementary Figure 10. (A) Quantitative RT-PCR results showing transcripts level of MHC class II genes comparing AM38-NTC cells and ERK1 KO or ERK2 KO cells. Data are presented as mean ± SD (n = 4). (B) HLA-DR protein expression was measured by flow cytometry-based analysis. Data are presented as mean ± SD (n = 4), unpaired two-tailed T test was used, and corresponding P-values are shown in the figure. (C) Quantitative RT-PCR results showing transcripts level of *Ciita* comparing QPP7-NTC cells and Erk1 KO or Erk2 KO cells. Data are presented as mean ± SD (n = 4), unpaired two-tailed T test was used. (D) Quantitative RT-PCR results showing transcripts level of MHC class II genes comparing QPP7-NTC cells and Erk1 KO or Erk2 KO cells. Data are presented as mean ± SD (n = 4), unpaired two-tailed T test was used, and corresponding P-values are shown in the figure.