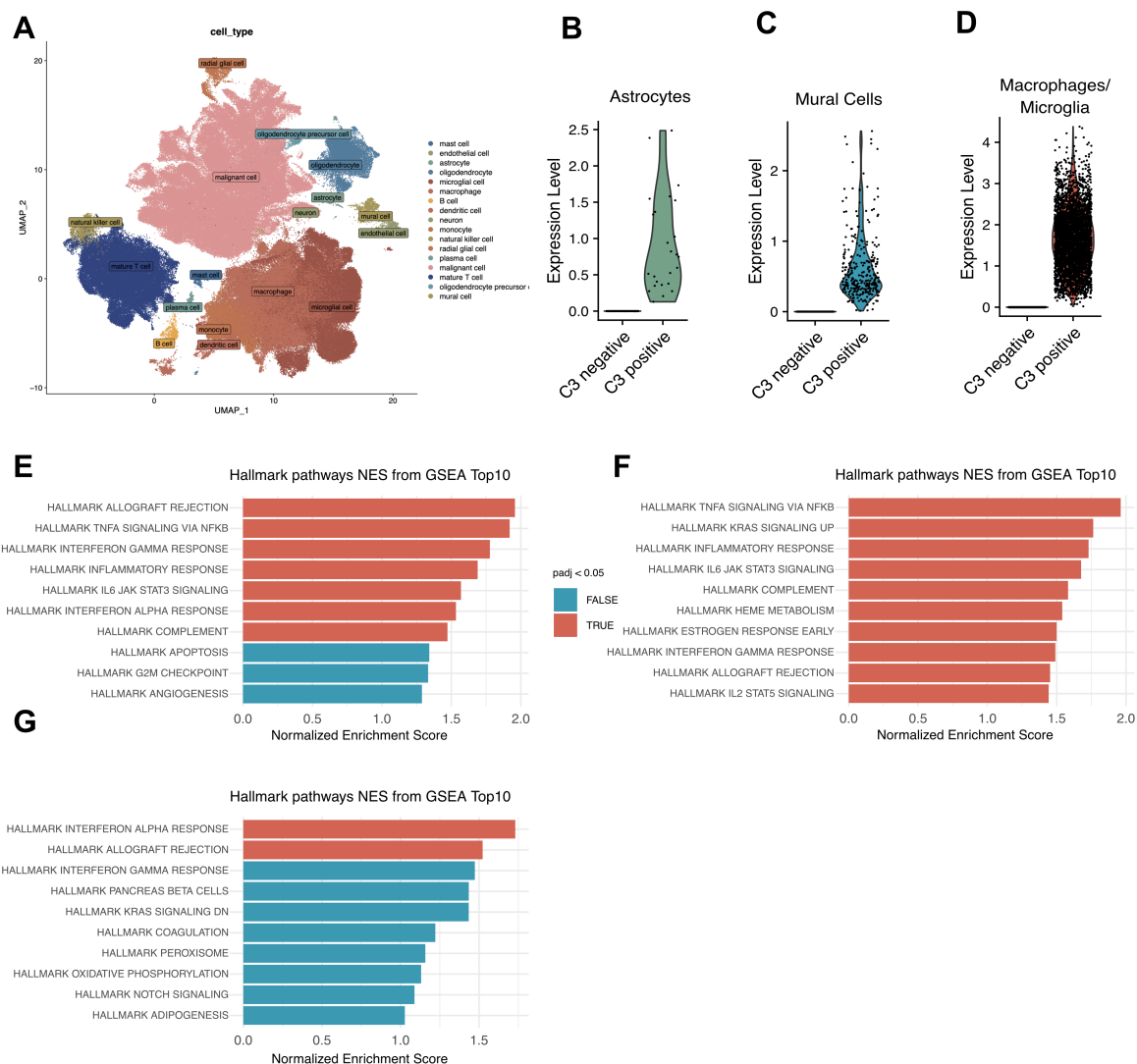


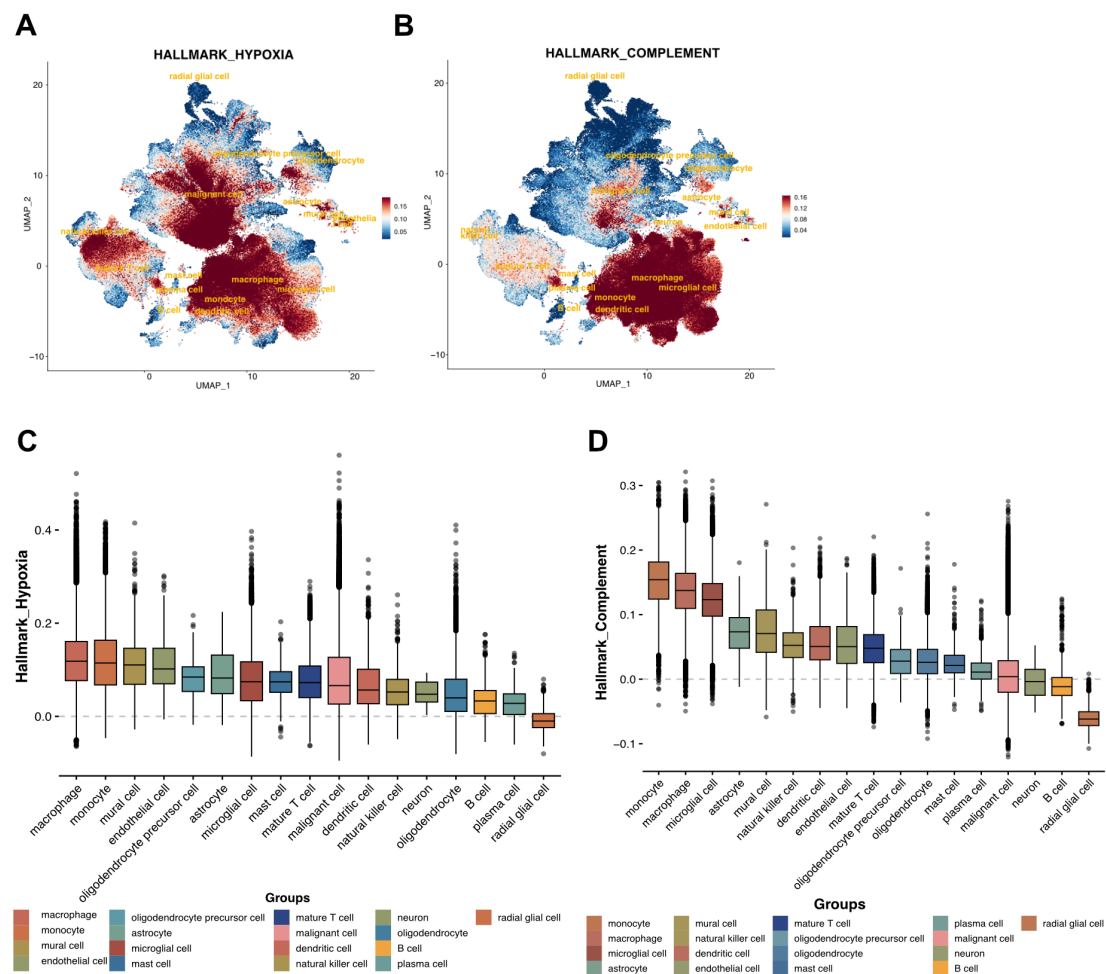
Supplemental Data.

Rosberg et al., Hypoxia-induced Complement Component 3 Promotes Aggressive Tumor Growth in the Glioblastoma Microenvironment



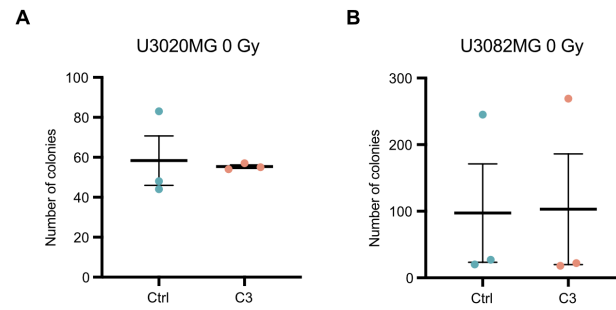
Supplemental Figure 1.

A, GBmap from Ruiz-Moreno, et al. 2022 (BioRxiv) comprising 16 data sets from 110 patients. **B-D**, C3 transcript level subdivided into C3-expressing or non-expressing cells from astrocytes, mural cells and macrophages/microglia. **E-G**, Hallmark enriched gene signatures in C3⁺ cells from astrocytes, mural cells and macrophages/microglia origin. Red- and blue-colored bars indicate significant and non-significant Benjamini-Hochberg adjusted *P* values (*padj* < 0.05), respectively.



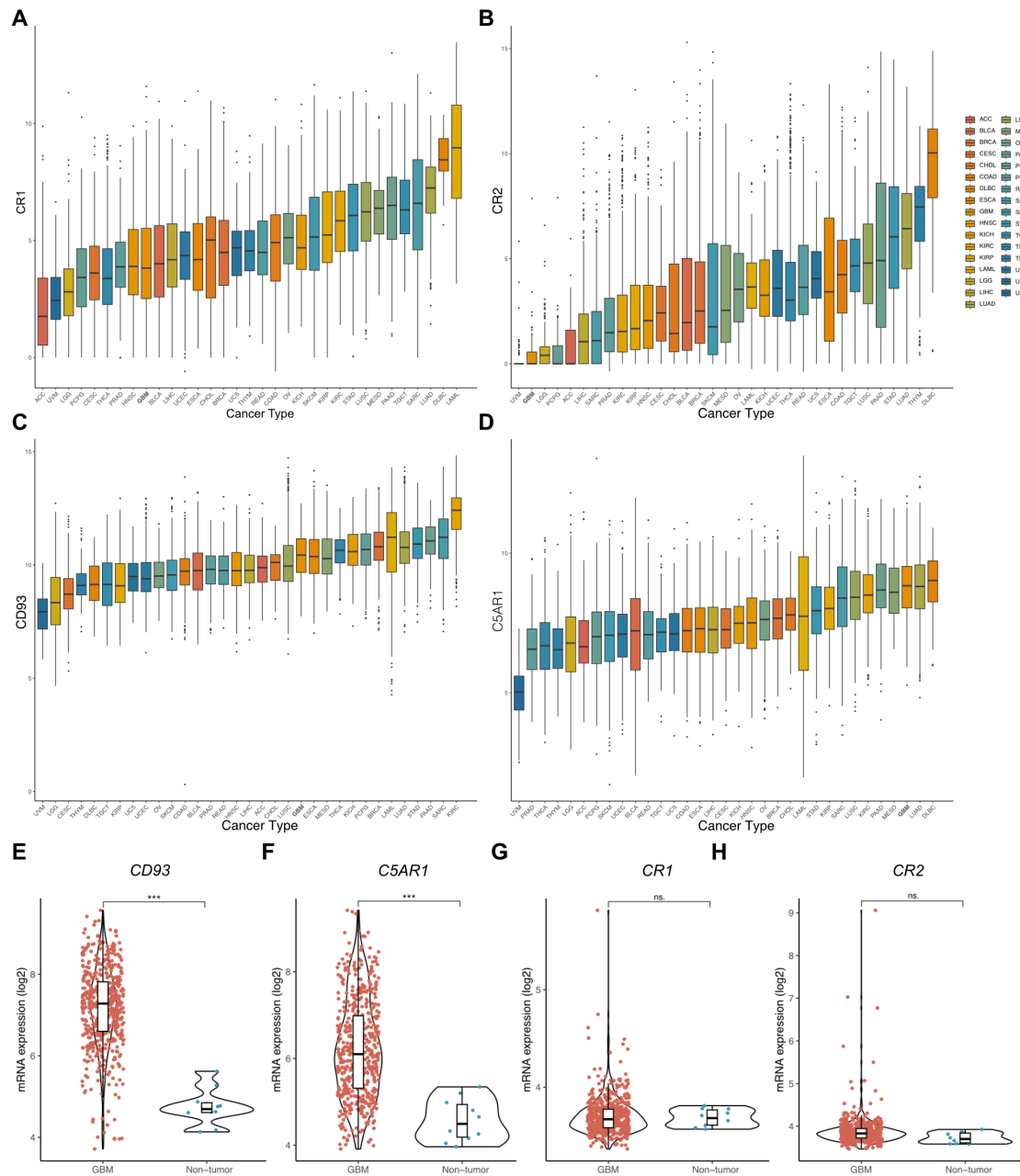
Supplemental Figure 2.

A, UMAP displaying Hallmark hypoxia gene signature mapped onto GBmap. **B**, UMAP displaying Hallmark complement gene signature mapped onto GBmap. **C-D**, Cell types expressing hypoxic and complement gene signatures in GBM. Color scale in A-B and values in C-D indicate hypoxia and complement module scores.



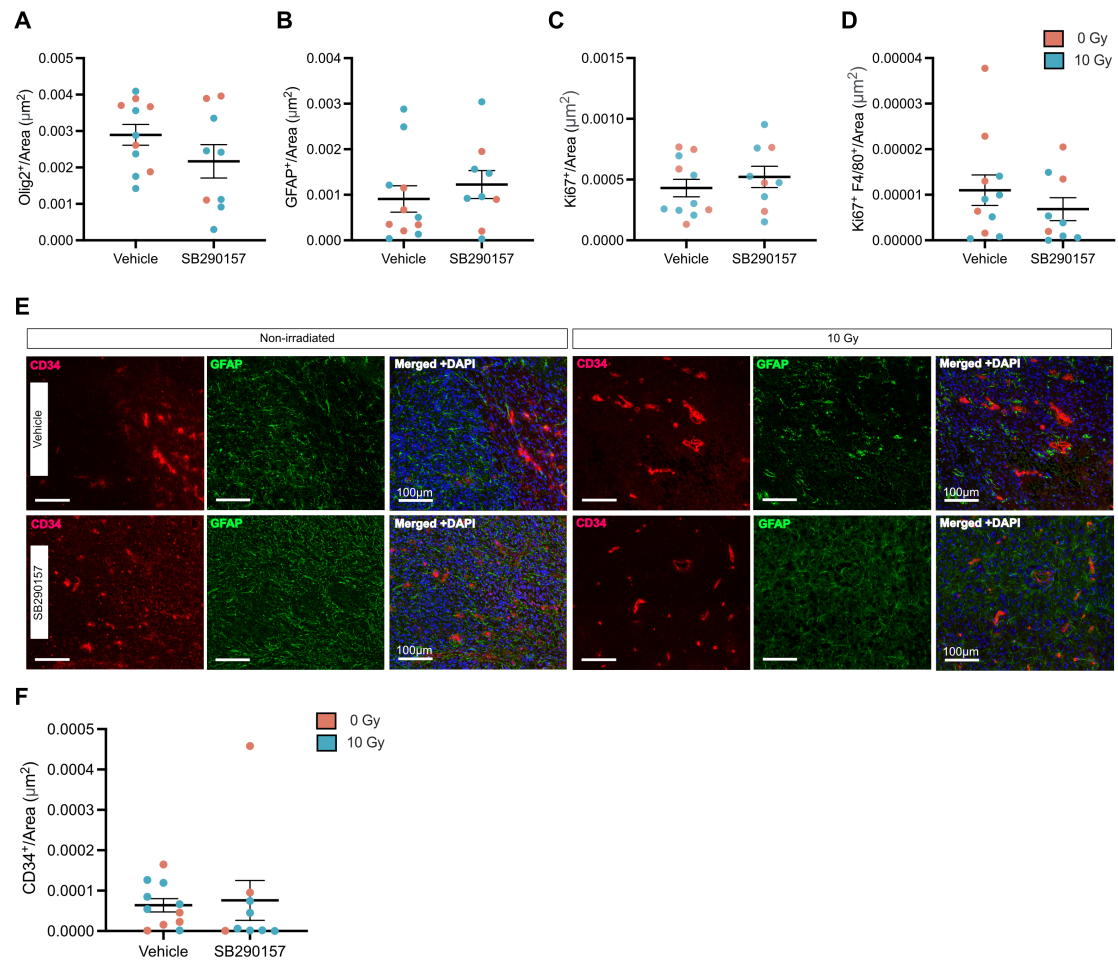
Supplemental Figure 3.

A-B. Quantification of number of colonies in U3020MG and U3082MG with or without presence of human C3 (180 ng/ml) in absence of irradiation.



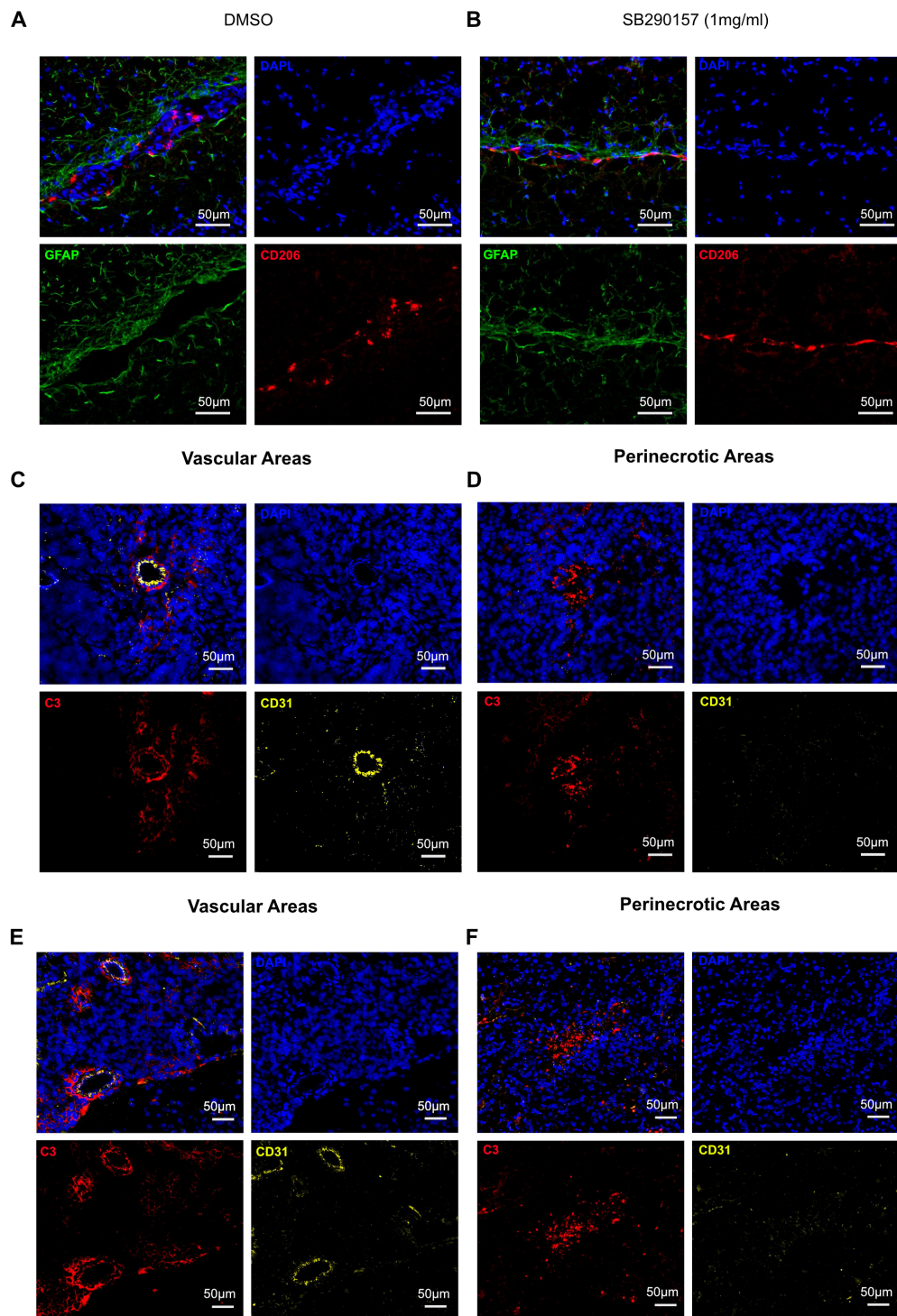
Supplemental Figure 4.

A-D, CR1, CR2, CD93 and C5AR1 transcript expression of Pan-Cancer TCGA data of common cancer types ($n=33$). **E-H,** CR1, CR2, CD93 and C5AR1 transcript expression in GBM compared to normal tissue. Statistical analysis were performed with Tukey's Honest Significant Difference (HSD).



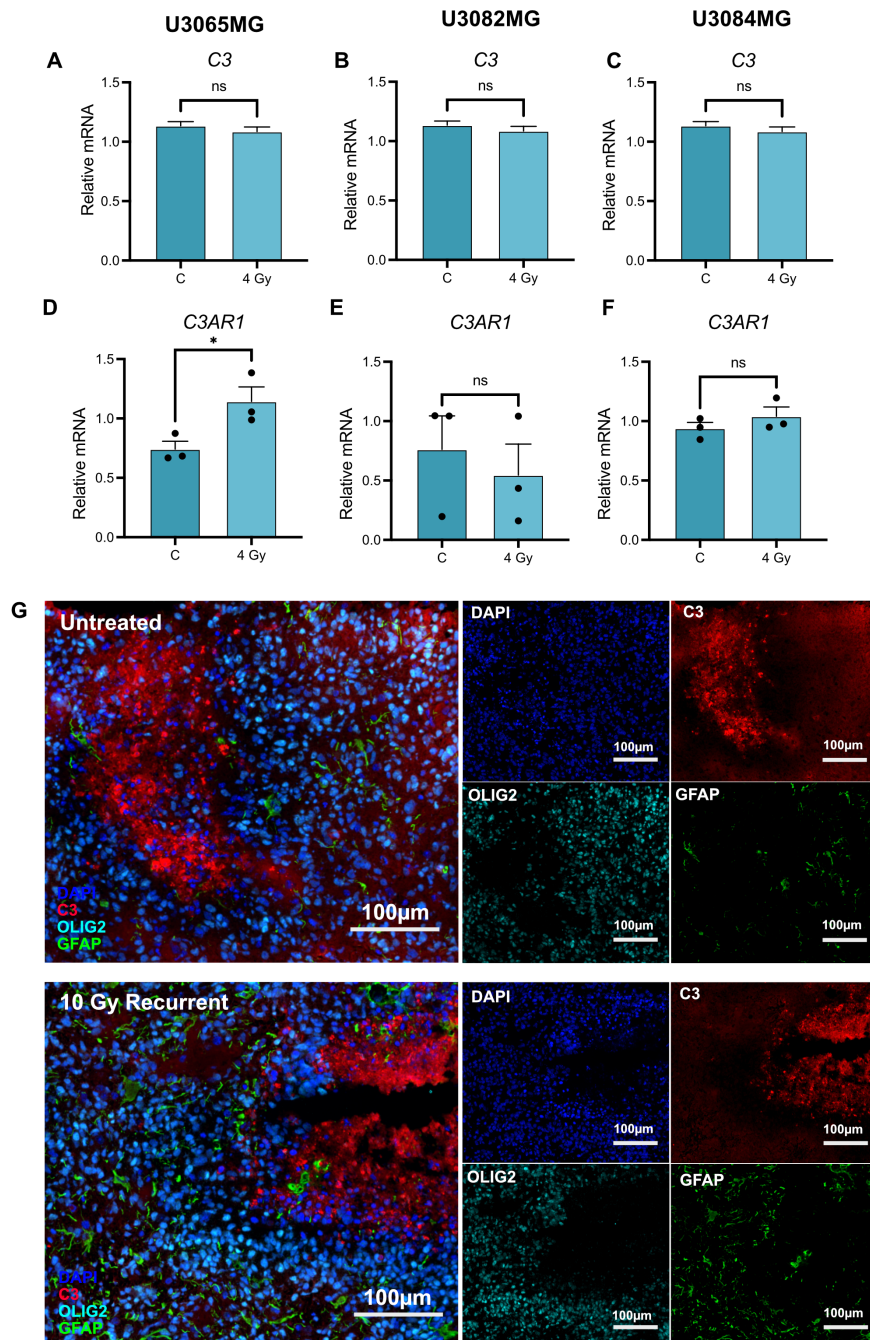
Supplemental Figure 5.

A-B, Quantitative analysis of Olig2⁺ or GFAP⁺ cells/Area (μm^2) from Vehicle or SB290157 from immunofluorescent staining in figure 5C. **C**, Representative immunofluorescent staining of vessels (CD34) and astrocytes (GFAP) in SB290157 treated mice. **H**, Quantitative analysis of CD34⁺ cells/Area (μm^2) from Vehicle or SB290157. Statistical analysis were performed with Mann-Whitney U test for treatments. *, $P < 0.05$, **, $P < 0.01$, or ***, $P < 0.001$.



Supplemental Figure 6.

A-B. Representative images of immunofluorescent staining of CD206+ cells in perivascular areas (CD31+) of non-tumor bearing mice injected with 1mg/ml SB290157 (n=4) or vehicle (n=4). **C-D.** Representative images of immunofluorescent staining of C3 in vascular and perinecrotic areas of SB290157 treated mice. **E-F.** Representative images of immunofluorescent staining of C3 in vascular and perinecrotic areas of 10 Gy + SB290157 treated mice.



Supplemental Figure 7.

A-F. Expression of C3 and C3AR mRNA in human primary glioma cells U3020 and U3082 in response to 3 Gy irradiation. Error bars represent SEM. *, $P < 0.05$, **, $P < 0.01$, or ***, $P < 0.001$. Statistical tests were unpaired t-test. **G.** Representative images of immunofluorescent staining of C3 from untreated or 10 Gy treated glioma bearing mice ($n=5$).