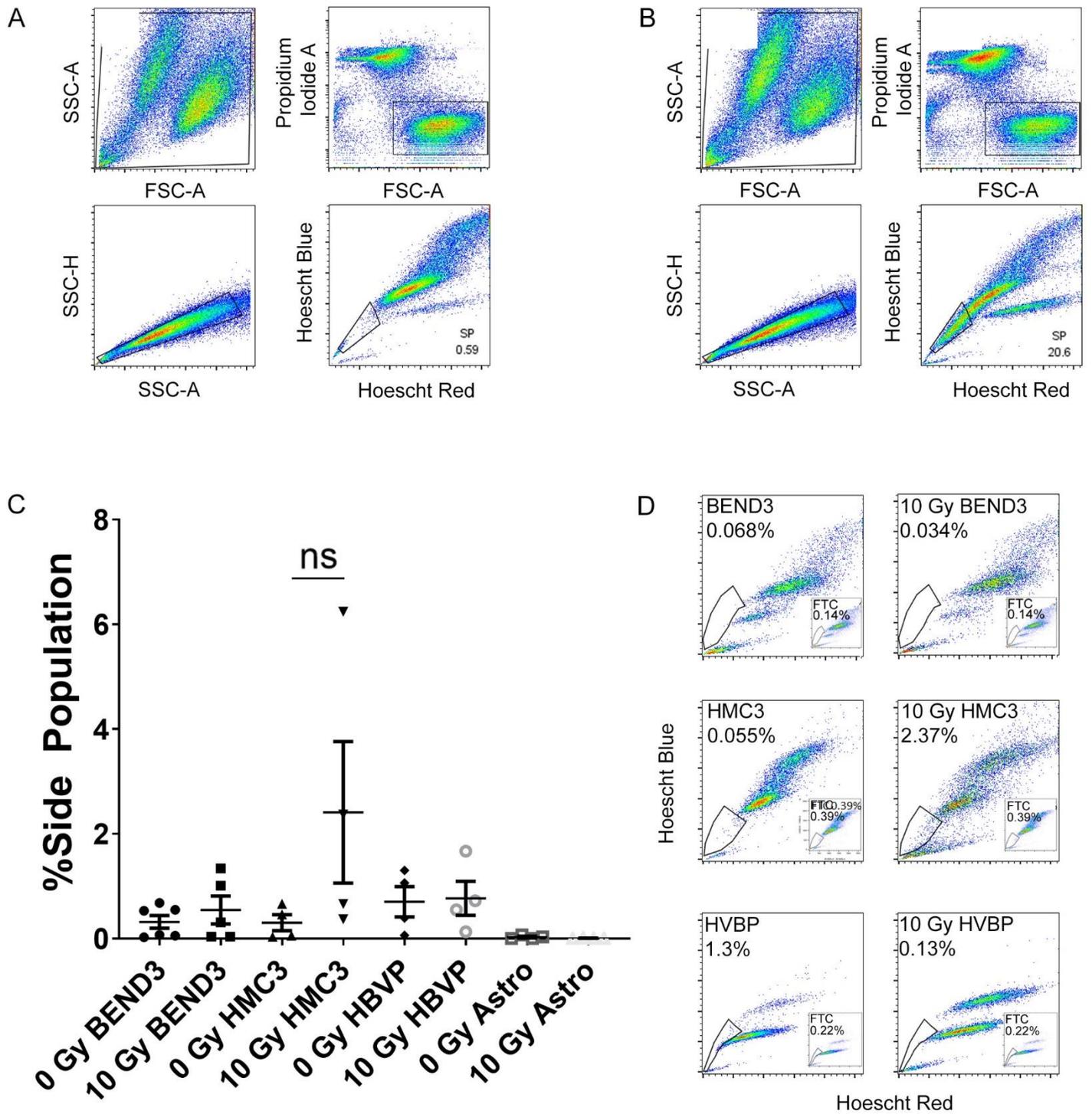
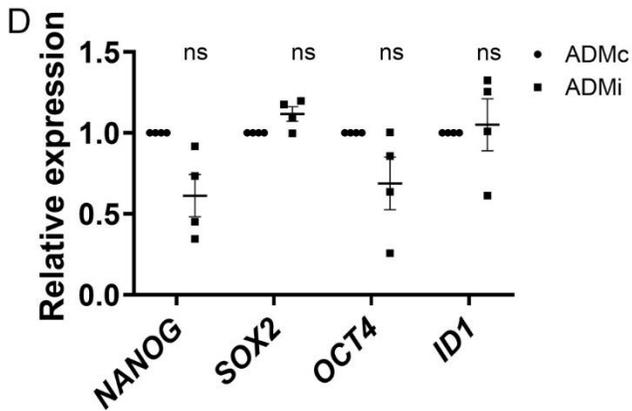
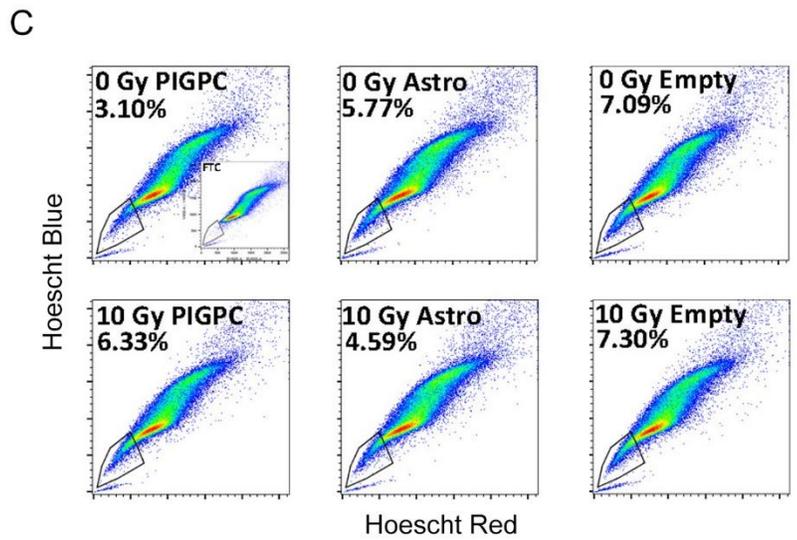
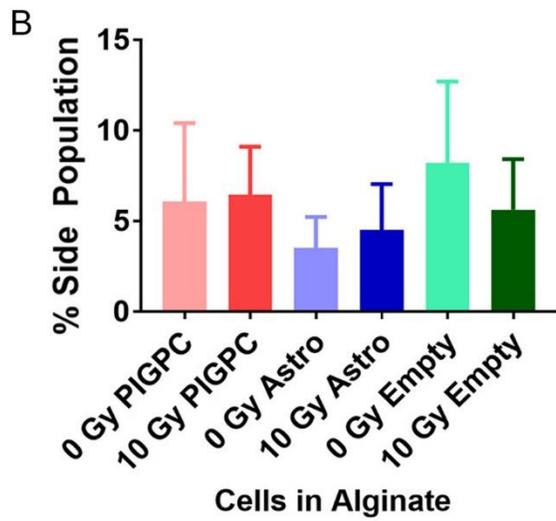
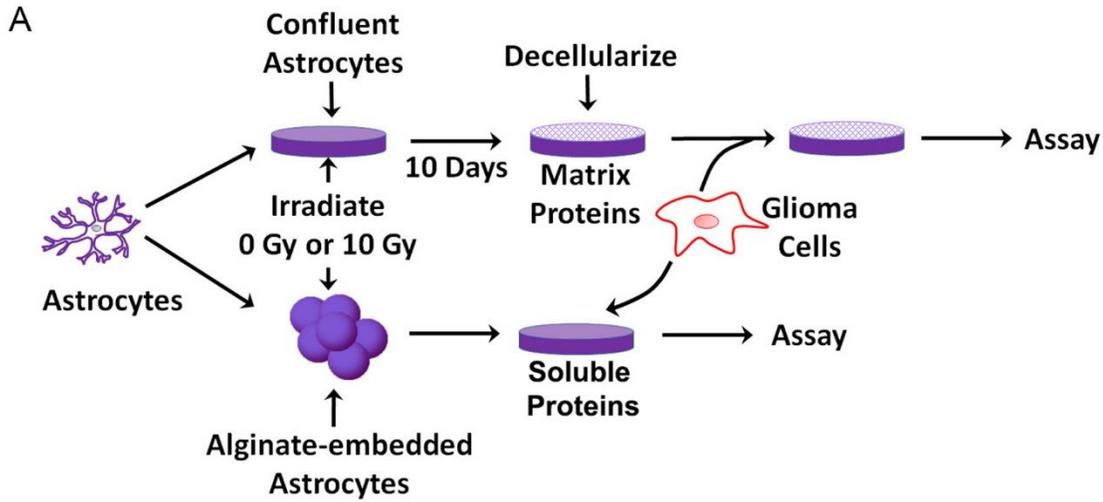


## Supplemental Figure 1



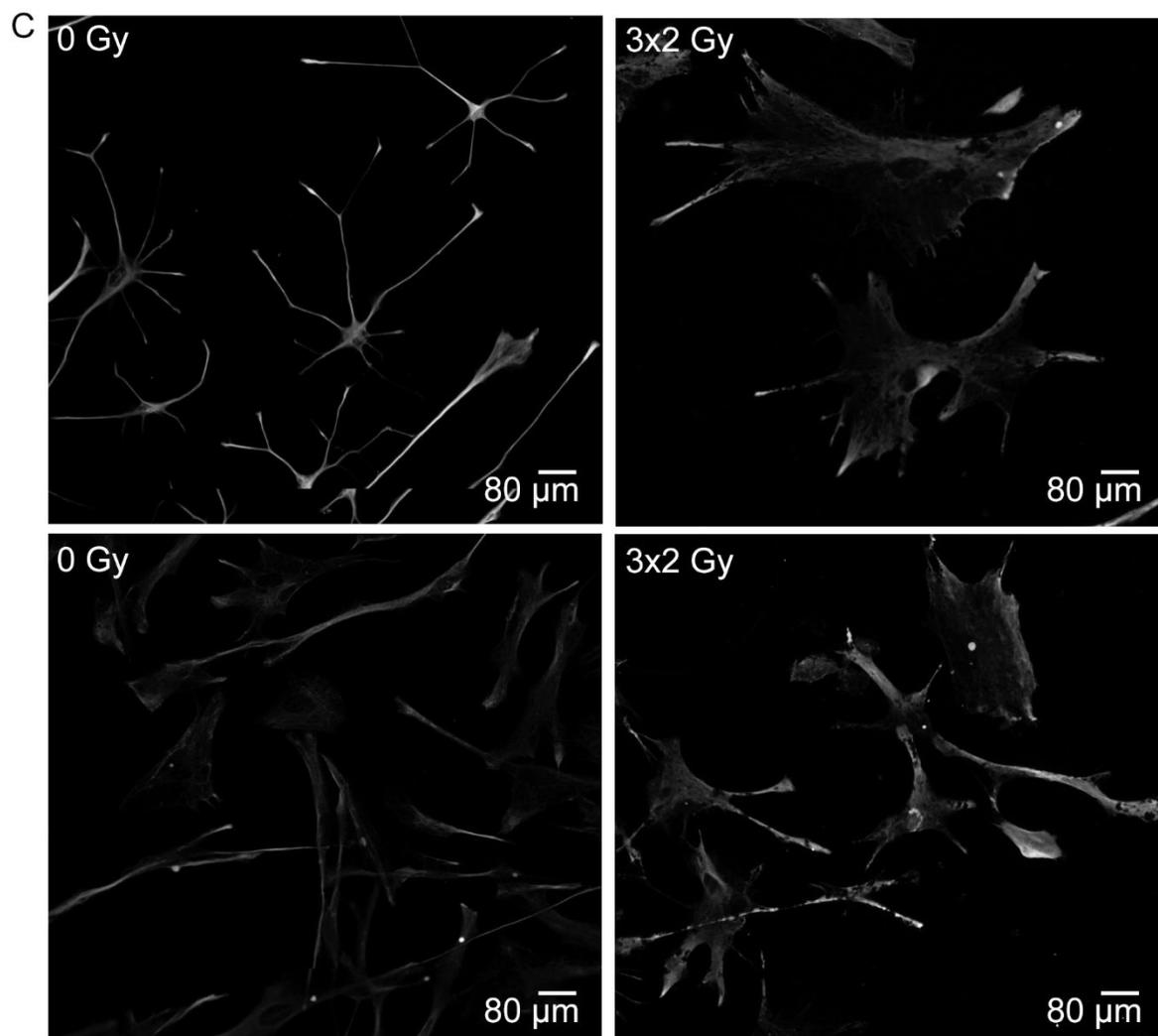
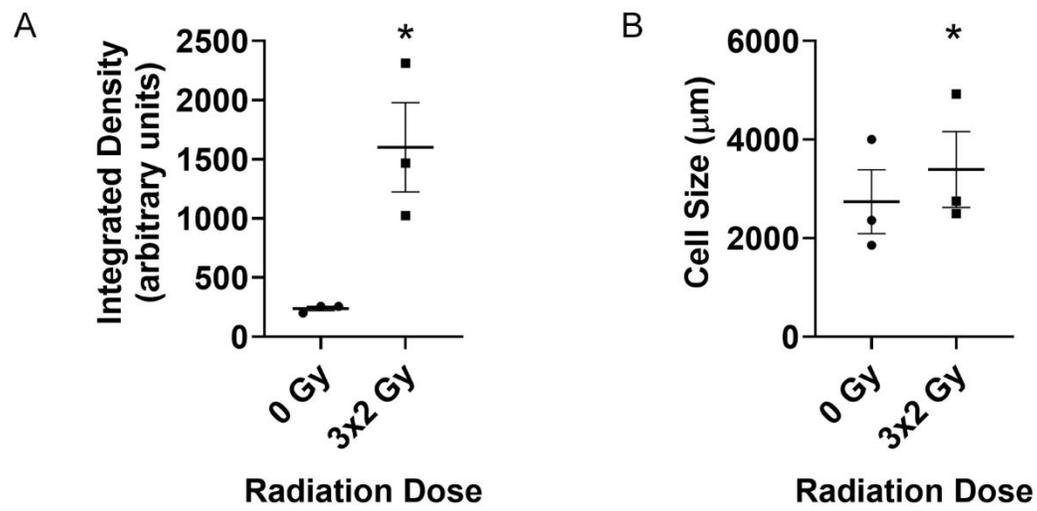
**Supplemental Figure 1. Stromal cells do not have a detectable side population.** A-B) Sample gating strategy for SP. A) Gating strategy for FTC control delineating side population gate. B) Sample of gating strategy on co-culture of PDGFB and astrocytes with applied SP gate from A. C) Average SP after treatment with either 0 Gy or 10 Gy on the indicated cell type. Error bars indicate SEM. D) Sample FACS plots show gating for SP.

Supplemental Figure 2



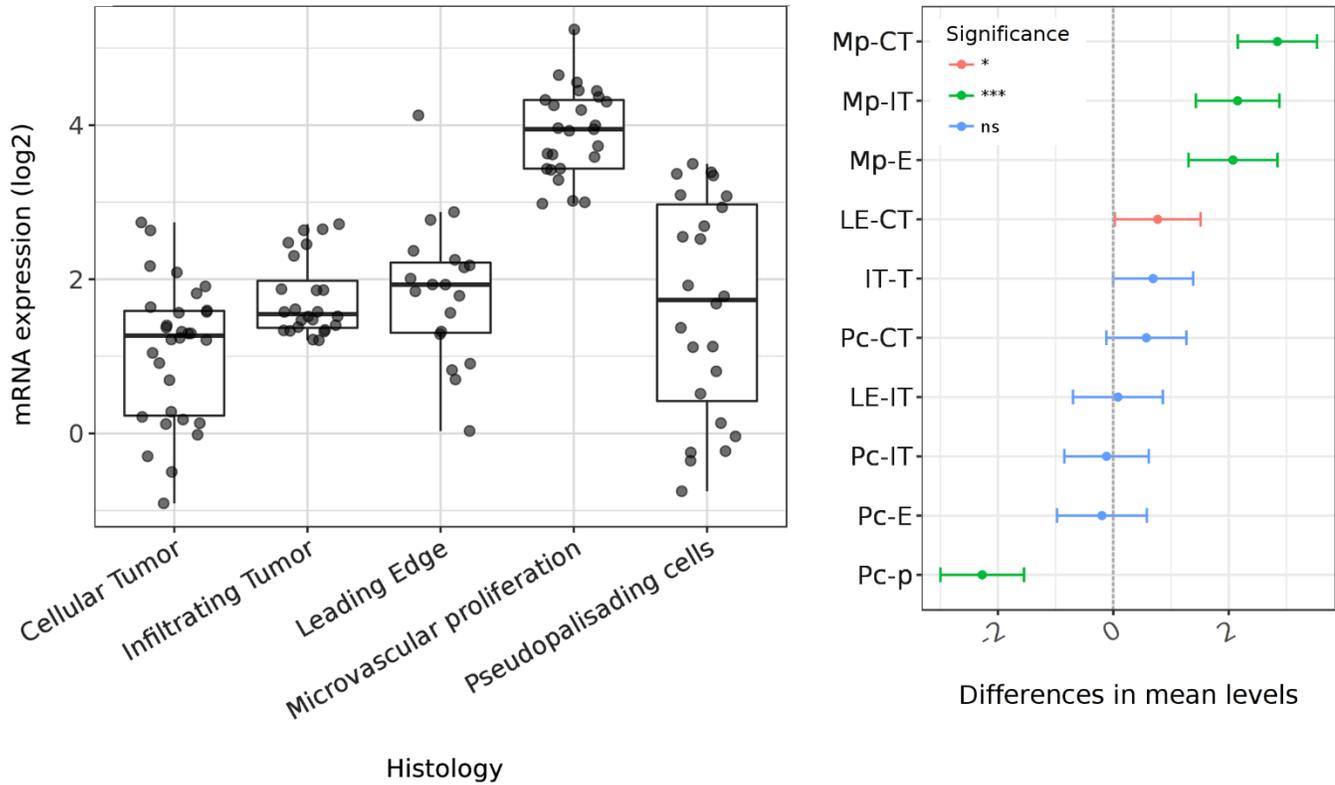
**Supplemental Figure 2. Conditioned media from astrocytes does not stimulate SP of glioma cells and there is no detectable change in stemness marker mRNA expression in U3082 cultured on ADMc versus ADMi.** (A) Experimental design showing two pathways for examining the effect of either astrocyte-derived soluble proteins or insoluble matrix proteins on glioma cells: Generation of astrocyte derived matrix (ADM) from control or irradiated astrocytes (ADMc and ADMi respectively); or suspension in sodium alginate to produce conditioned medium. (B) Average SP of glioma cells after co-culture with sodium alginate beads embedded with either PIGPC, astrocytes (Astro), or no cells (Empty). PIGPC, astrocytes, and empty sodium alginate beads were pretreated with either 0 Gy or 10 Gy. Error bars indicate SEM. (C) Sample FACS plots show gating for SP. (D) Scatter plot showing expression of indicated genes in U3082 cells cultured on ADMc or ADMi. Dots indicate values relative to ADMc control. Bars indicated average from n=4 samples. Error bars are SEM. ns indicates not significant.

Supplemental Figure 3



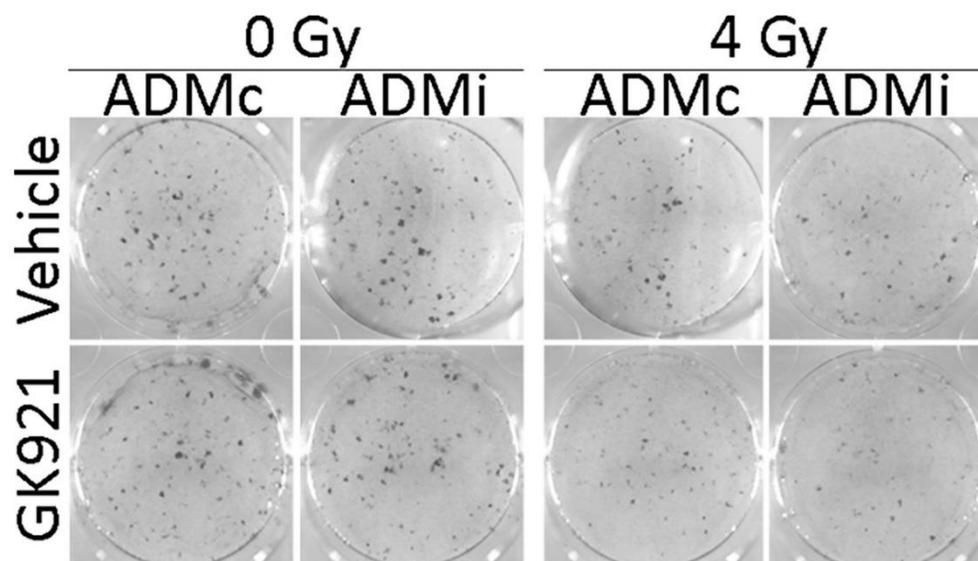
**Supplemental Figure 3. Fractionated radiation doses stimulate increased vimentin expression and somatic hypertrophy.** (A) Scatter plot showing integrated density of vimentin staining in astrocytes after treatment with 0 Gy or 3x2 Gy. Dots represent values measured in astrocytes derived from three individual donors. Bars indicate mean of n=3 experiments. Error bars are SEM. \*  $P \leq 0.05$ , t-test. (B) Scatter plot of cell size measured in vimentin-positive astrocytes after treatment with 0 Gy or 3x2 Gy. Dots represent values measured in astrocytes derived from three individual donors. Bars indicate mean of n=3 experiments. Error bars are SEM. \*  $P \leq 0.05$ , ratio paired t-test. (C) Immunofluorescent detection of vimentin in astrocytes treated with 0 Gy or 3x2 Gy.

Supplemental Figure 4



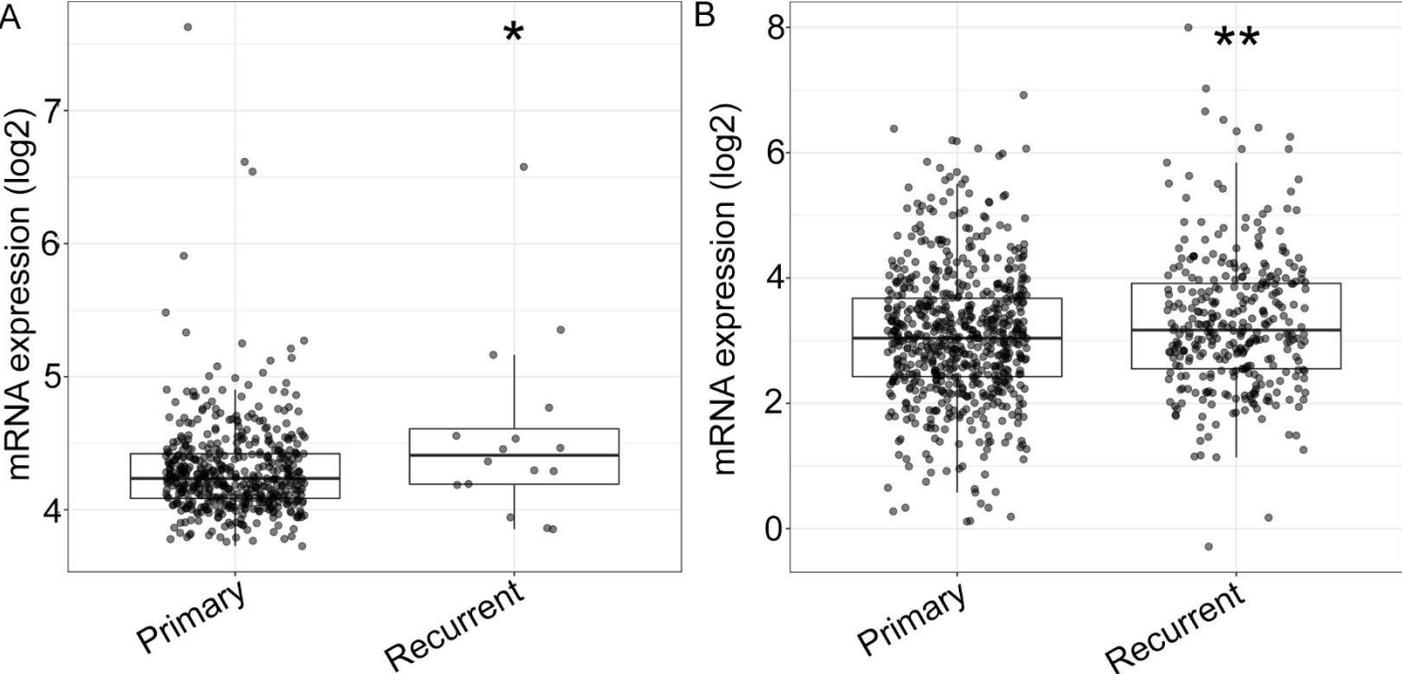
**Supplemental Figure 4. TGM2 is elevated in areas of microvascular proliferation.** TGM2 transcript expression in the indicated histological region of gliomas (left) and statistical analysis (Tukey's Honest Significant Difference, right). Microvascular proliferation (Mp), Cellular Tumor (CT), Infiltrating Tumor (IT), Leading Edge (LE), Pseudopalisading cells (Pc).

Supplemental Figure 5



**Supplemental Figure 5. GK921 inhibits colony formation on ADMi after irradiation.** Example colonies of clonal survival of U251 glioma cells plated on ADMc or ADMi in triplicate wells in media containing vehicle or 0.1  $\mu\text{M}$  GK921, followed by irradiation with 0 Gy or 4 Gy.

Supplemental Figure 6



**Supplemental Figure 6. TGM2 mRNA is elevated in recurrent tumors.** Expression of TGM2 mRNA in human primary or recurrent GBM from the (A) TCGA and (B) CTGA GBM datasets.