**Supplementary Fig.1. The expression and survival curves of HAS1 and HAS2 different grades of glioma.** (A-B) Relative expression of the HAS1 and HAS2 mRNAs in patients with LGG and GBM from TCGA. Survival curves of HAS1 and HAS2 for patients with LGG and GBM from TCGA database. Data are presented as means ± SD; \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001.

**Supplementary Fig.2. Interfering with HAS3 and CD44 suppress glioma cell proliferation in vitro and in vivo.** (A) Relative HA content in U251 and LN229 glioma cells transfected with the HAS3 siRNA. (B) Levels of the Ki67 protein in U251 glioma cells were detected using immunofluorescence staining after transfection with the HAS3 siRNA or treatment with the CD44 antibody for 48 h. Scale bar: 50 μm. (C) Gene knockout efficiency of the HAS3 siRNA and CD44 siRNA. (D) Representative images of the subcutaneous xenograft tumors from the control and lentivirus HAS3 siRNA or lentivirus CD44 siRNA stably transfected glioma cell groups. (E) The tumor volume of the subcutaneous xenograft tumors from the control and lentivirus HAS3 siRNA or lentivirus CD44 siRNA stably transfected glioma cell groups. Data are presented as means ± SD; \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001.

**Supplementary Fig.3. 4-MU suppress glioma cell proliferation in vitro and in vivo.** (A) Relative levels of the P62 and LC3 proteins in U251 glioma cells transfected with the HAS3 siRNA, followed by treatment with HA (25 µg/ml) for 48 h. (B) Relative HA content in U251 and LN229 glioma cells treated with 4-MU for 48 h. (C) Levels of the Ki67 protein in U251 glioma cells were detected using immunofluorescence staining after treatment with 4-MU for 48 h. Scale bar: 50 μm. (D) Viability of the U251 glioma cell line cultured with 4-MU, followed by treatment with HA (25 µg/ml) for 48 h. (E) Relative levels of the P62 and LC3 proteins in U251 glioma cells cultured with 4-MU, followed by treatment with HA (25 μg/ml) for 48 h. (F) The percentage of Ki67-positive U251 glioma cells cultured with 4-MU, followed by treatment with CQ (30 mmol/L) for 48 h. (G-H) Representative images and volumes of the subcutaneous xenograft tumors from the control and 4-MU treatment groups. Data are presented as means ± SD; \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001.