

Supplementary Figure 1.

1. Western blot shows the ectopic expression level of IDH1 mutants and endogenous IDH1 wild type in U251. DOX, doxycycline; \*, endogenous IDH1 protein.
2. MitoSOX immunofluorescence imaging shows the mitochondrial ROS level in IDH1-mutatd U251 cells, with the treatment of ROS clelators mannitol (50mM, 24 hr), catalase (500 U/ml, 24 hr) and MnTBAP (50 µM, 2 hr). Bar = 10 µm.
3. Western blot shows the apoptotic marker cleaved caspase 3 level in U251 IDH1 R132H cells after knockdown of GCLC and GCLM. C3, caspase 3; cC3, cleaved caspase 3.
4. Western blot shows the apoptotic marker cleaved caspase 3 level in U251 IDH1 R132H cells after knockdown of GCLC and GCLM, with the rescue of catalase (500 U/ml, 24 hr). siGCLC.1 and siGCLM.1 were used.
5. Western blot shows the knockdown efficiency of small interference RNA targeting Nrf2 in U251 cells.
6. Mouse body weight was measured after brusatol treatment. Bru, brusatol; NAC, N-acetylcysteine.
7. Western blot shows the knockdown efficiency of small interference RNA targeting GCLC and GCLM in U251 IDH1 R132H cells.
8. Real-time PCR shows the knockdown efficiency of small interference RNA targeting GCLC and GCLM in U251 IDH1 R132H cells.



Supplementary Figure 2.

1. ROS-Glo assay measures the ROS level in GSC827 and TS603 after brusatol (40nM, 24 hr) and Catalase (500 U/ml, 24 hr) treatment. \*\*\*, p < 0.001.
2. Real time PCR shows the mRNA level of NFE2L2, GCLM and SLC7A11 in GSC827, GSC923 and TS603 cells. \*\*\*, p < 0.001.
3. GSH/GSSG assay measures the GSH and GSSG level in GSC827, GSC923 and TS603 cells. \*\*\*, p < 0.001.
4. Annexin-PI flow cytometry staining shows the apoptotic cells in GSC827, GSC923 and TS603 after brusatol (40nM, 72 hr) treatment.
5. Quantification of apoptotic cells in GSC827, GSC923 and TS603 after brusatol (40nM, 72 hr) treatment. \*\*, p < 0.01.