**Legends of Supplemental Figures:**

**Figure S1. B7-H3 knockdown reduces glucose uptake and lactate production in breast cancer cells.** Cells treated with CoCl2 for 24 h, which is a treatment commonly used to mimic hypoxia conditions by preventing HIF hydroxylation. (A) Glucose uptake and (B) lactate production were measured in B7-H3 knockdown cells. (±SE, three independent experiments; \*p<0.05)

**Figure S2. B7-H3 is susceptible to glycolysis inhibition. Growth inhibition and colony formation were conducted.** (A) A specific glycolysis inhibitor, oxamate, greatly inhibited the growth of all the cells in a dose-dependent manner In the MDA-MB-231 and MDA-MB-435 shB7-H3 cells. However, the growth of B7-H3 knockdown cells was less inhibited. (B) Colony formation assay in medium with or without oxamate in MDA-MB-468 B7-H3 cells. Cells were diluted and seeded at about 1000 cells per well of a six-well plate. After a 12-h incubation, cells were treated with or without oxamate. After incubation for 7 days, cells were washed with PBS twice, fixed with methanol for 15 min, and stained with 0.5% crystal violet for 15 min at room temperature and then measured. B7-H3 was more senstive to oxamate treatment (±SE, three independent experiments; \*\*p<0.05; \*\*\*p<0.01).

**Figure S3. B7-H3 knockdown reduces sensitivity to glucose deprivation.** In the MDA-MB-231 and MDA-MB-435 shB7-H3 cells, proliferation assay was conducted. (A) Proliferation assay in medium with or without glucose. (B) Proliferation assay in medium with glucose and galactose. (±SE, three independent experiments).

**Figure S4. B7-H3 knockdown reduces protein levels of HIF-1α.** Cells were transiently downregulated by a siRNA against B7-H3. Protein levels of HIF-1α were measured in CoCl2 treatment for 24 h or not.

**Figure S5. B7-H3 does not affect mRNA levels of HIF-1α.** mRNA levels of HIF-1α were measured in MDA-MB-231 and MDA-MB-435 B7-H3 knockdown cells. (±SE, three independent experiments).

**Figure S6. B7-H3 Mediated ROS are reduced by ROS scavenger.** (A) MDA-MB-468 B7-H3 overexpressing cells grown under hypoxia conditions were incubated in absence or presence of PEG-catalase (500U/ml, pretreated for 1h before hypoxia) and then trypsinized and labeled with CellROX and MitoSOX to measure ROS levels by flow-cytometry. (B) MDA-MB-468 B7-H3 overexpressing cells grown under hypoxia conditions were incubated in absence or presence of NAC (10 mM, pretreated for 1h before hypoxia) and then trypsinized and labeled with CellROX and MitoSOX to measure ROS levels by flow-cytometry.(±SE, three independent experiments; \*p<0.05; \*\*p<0.01).

**Figure S7. B7-H3 affects pentose phosphate pathway and reduces SOD activity.** (A) Glucose-6-phosphate dehydrogenase (G6PD) activity assay in MDA-MB-231 shB7-H3 and MDA-MB-468 B7-H3 cells. Cells were incubated in hypoxia for 24 hour and then G6PD activity was measured. B7-H3 induced G6PD activity under hypoxia condition. (B and C) SOD activity assay in MDA-MB-231 shB7-H3 and MDA-MB-468 B7-H3 cells. The sensitive SOD assay kit (BioVision) utilizes WST-1 that produces a water-soluble formazan dye upon reduction with superoxide anion. The rate of the reduction with a superoxide anion is linearly related to the xanthine oxidase (XO) activity, and is inhibited by SOD. We regard value of formazan dye without samples as 0%. Cells were incubated in hypoxia for 24 hour and then cytosolic and mitochondrial SOD activity were measured. Cytosolic and mitochondrial lysates (10 ug) were used to determine SOD activity. B7-H3 reduced mitochondrial SOD activity under hypoxia condition. (±SE, three independent experiments; \*p<0.05; \*\*p<0.01; \*\*\*p>0.001).

**Figure S8. B7-H3 knockdown reduces sensitivity to ROS inhibition.** Cells were cultured with or without NAC and then measured growth rates.

**Figure S9. B7-H3 knockdown reduces protein levels of HIF-1α and its downstream targets, LDHA and PDK1.** Immunohistochemistry analysis of xenograft tumors with MDA-MB-231 shB7-H3 cells was conducted. Sections were stained with B7-H3, HIF-1α, LDHA and PDK1.