



Figure S4: Combined loss of CAIX activity and the GSH synthesis axis of Gln metabolism increases cytotoxicity of hypoxic cancer cells.

(A) Cell cytotoxicity data of SUM159PT cells with the combination of Compound 11 and CB839 at indicated concentrations at 1% O_2 for 72 h. Bars indicate means \pm SD.

Synergy scores and interpretation of the score are provided in boxed insets for each graph. The statistical significance was assessed using two-way ANOVA. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. **(B)** Cellular ROS level in 4T1Luc cells measured using CM-H2DCFDA with (+) or without (-) 50 μM SLC-0111 at 1% O_2 for 72 h. Bars indicate means \pm SD. Statistical significance was assessed using Mann Whitney test. ** $p < 0.01$. **(C)** GSH to GSSG ratio in SUM159PT cells cultured with (+) or without (-) 100 μM SLC-0111 in 1% O_2 for 72 h. Statistical significance was assessed using an unpaired t-test. ** $p < 0.01$.