



**Figure S2: CAIX catalytic activity and intracellular domain regulate Gln uptake.**

**(A)** Cellular expression of SLC1A5 and CAIX shown by Western blotting in cell lysates from the indicated cell lines with the treatment of SLC-0111 at indicated concentrations.

**(B)** Gln uptake in SUM159PT cells treated with SLC-0111 (100 μM), 13 - Compound 13 (50 μM) or 11 -Compound 11 (2 μM).

**(C)** Gln uptake in SUM159PT wild type (WT) and CAIX mutant cell lines exogenously expressing full length CAIX (FL), intracellular domain truncated CAIX (ΔIC) or catalytically inactive CAIX (H200A).

All treatments were carried out at 1% O<sub>2</sub> for 72 h prior to the assay. For graphs, bars indicate means ± SD. Statistical significance was assessed using one-way ANOVA; \*p < 0.05, \*\*\*\*p < 0.0001; ns, non-significant.