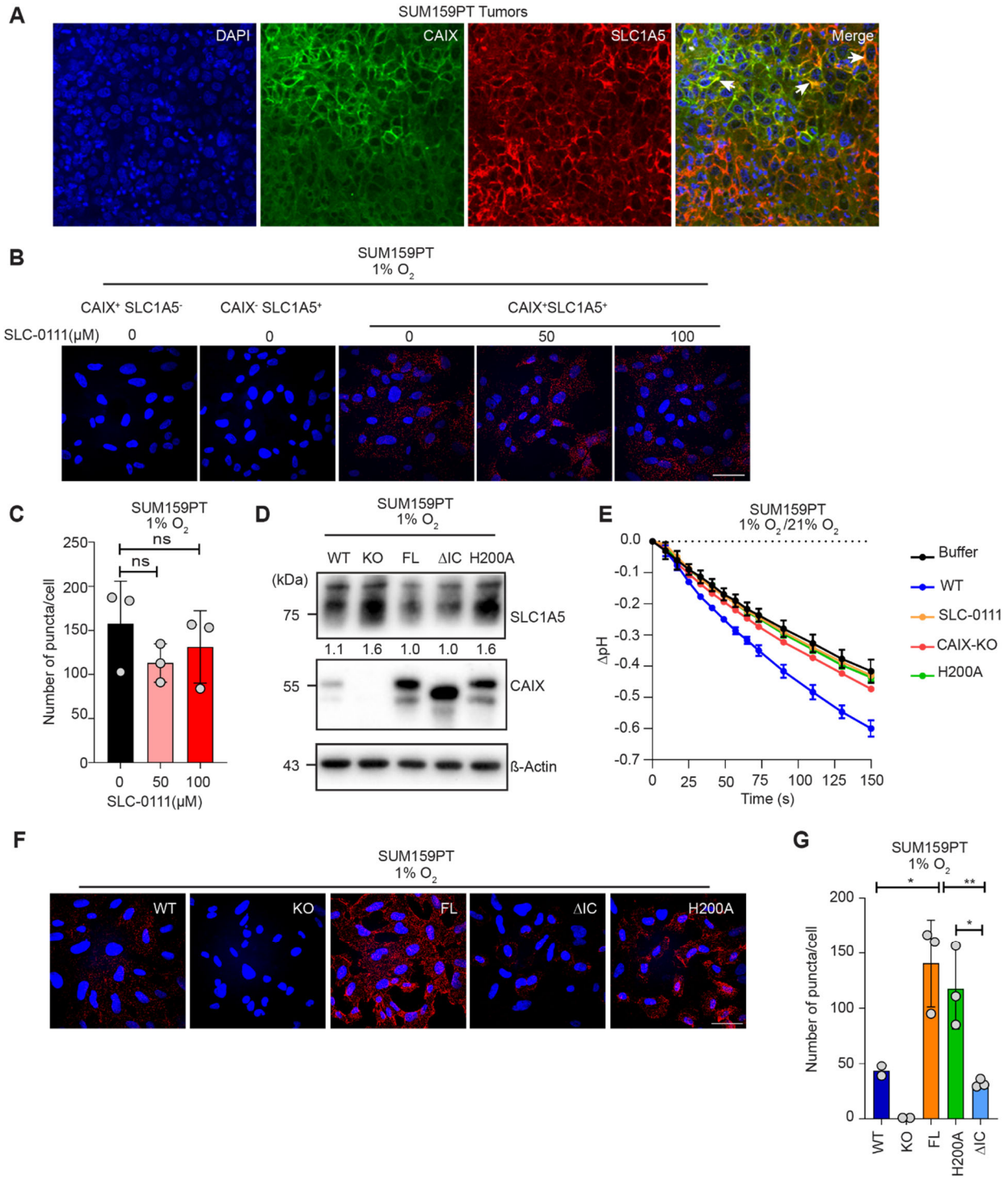

Figure S1: Characterization of the interaction between SLC1A5 and CAIX. **(A)** Representative images of SUM159PT tumor tissue sections stained by immunofluorescence for CAIX (green) and SLC1A5 (red). Merged image shows regions of co-localization (arrows). **(B)** Interaction of SLC1A5 and CAIX (Red puncta) in SUM159 cells at indicated concentrations of SLC-0111 shown by PLA. Treatments with only SLC1A5 antibody ($CAIX^{-}$ $SLC1A5^{+}$) and only CAIX antibody ($CAIX^{+}SLC1A5^{-}$) were

used as negative controls for the assay. Scale bar, 50 μM. **(C)** Quantification of the PLA signal from three images for each condition shown in (B), having at least 20 cells in each image. **(D)** Cellular expression of SLC1A5 and CAIX shown by Western blotting in cell lysates from SUM159PT WT, *CA9*^{KO}, and CAIX mutant cell lines exogenously expressing full length CAIX (FL), intracellular domain truncated CAIX (ΔIC) or catalytically inactive CAIX (H200A). Quantification of relative levels of expression of SLC1A5, normalized to β-actin, is indicated below the blot. **(E)** CO_2-based carbonic anhydrase activity assay in SUM159PT cells indicated by the drop in pH in indicated conditions. SLC-0111, 50 μM. **(F)** Interaction of SLC1A5 and CAIX (Red puncta) in SUM159PT WT, *CA9*^{KO}, and CAIX mutant cell lines shown by PLA. Scale bar, 50 μm. **(G)** Quantification of the PLA signal from three images for each condition shown in (F), having at least 20 cells in each image.
All treatments were carried out at 1% O_2 for 72 h prior to the assay. In panel E, the endpoint assay was carried out in normoxia. For all graphs, bars indicate means ± SD. Statistical significance was assessed for (C and G) using one-way ANOVA; Kruskal-Wallis. *$p < 0.05$, **$p < 0.01$; ns, non-significant.