



**Supplementary Figure S3. MAPK/ERK and PTEN/PI3K modulation of macropinocytosis and albumin uptake.** **A-B**, Representative images (**A**, scale bar = 50 μm) and quantification (**B**) of 4 h albumin and dextran uptake in TPC1 papillary thyroid cancer cells transfected with empty vector (control), *BRAF*<sup>wt</sup> or *BRAF*<sup>V600E</sup> plasmid for 72h (n = 27 images from 3 independent experiments, using one-way ANOVA/Dunnett compared to control.). **C-D**, Representative images (**C**, scale bar = 50 μm) and counts (**D**) of dead cells (EthD-1 positive), live cells (Calcein AM positive) and total cells after 24 h treatment of DMSO control, dabrafenib, trametinib and the combination; data are means ± s.e., n = 12-13, using one-way ANOVA/Dunnett test compared to DMSO control. **E-G**, Representative images (**E**, scale bar = 50 μm) and quantification (**F**) of 4 h albumin and dextran uptake in Nthy-ori-3-1 follicular thyroid cells transfected with *KRAS*<sup>wt</sup> or *KRAS*<sup>G12D</sup> plasmid for 72h; data are means ± s.e., n = 9, using two-tailed t-tests. **G**, Representative immunofluorescence (scale bar, 50 μm) of p-ERK1/2 matching conditions in **E-F**. **H-I**, Representative images (**H**, scale bar = 50 μm) and quantification (**I**) of 4h albumin and dextran uptake in Nthy-ori-3-1 follicular thyroid cells that were pre-treated with PTEN-targeted pooled siRNA or control siRNA for 72 h; data are means ± s.e., n = 150 cells per cond., using two-tailed t-tests. **J**, Representative immunofluorescence (scale bar, 50 μm) of PTEN matching conditions in **H**. **K-N**, Representative images (**K**, **M**) and quantification (**L**, **N**) of 4h albumin and dextran uptake in FTC236 (**K-L**) and FTC133 (**M-N**) cells, after pretreatment with 3 μM serabelitinib and alpelisinib; data are means ± s.e., n = 90 per cond., using one-way ANOVA/Dunnett.