



**Supplemental Figure S2: PDAC cells grown on 2D tissue culture plastic exhibit increased sensitivity to MRTX1133 in 'low' confluent than in 'high' confluent 2D cultures.** **A, B.** PDAC cells were plated at 'low' ( $5 \times 10^4$  cells/well) or 'high' confluent ( $2.5 \times 10^5$  cells/well) in 12-well plates for 24 hours and treated with DMSO or MRTX1133 ( $0.5 \mu\text{M}$ ) for 8 hours. ERK activation was evaluated by Western blotting. Blots are representative of three biological replicates. **C.** PDAC cells were plated at 'low' ( $2 \times 10^3$  cells/well) or 'high' confluent ( $10 \times 10^3$  cells/well) in 96-well plates for 24 hours and treated with DMSO or MRTX1133 ( $0.25 \mu\text{M}$ ,  $0.5 \mu\text{M}$ ,  $1.0 \mu\text{M}$ ) for 72 hours. Cell viability was determined by MTT assay. Error bars  $\pm$  SD,  $n=3$ , unpaired t-test. \*,  $p < 0.05$ ; \*\*\*\*,  $p < 0.0001$ .