



### Supplementary Figure 3. Oncogenic Kras induces Nix expression in a MAPK pathway-dependent fashion.

A) Fold change in mRNA expression of mitochondrial biogenesis genes in LSL-KrasG12D MEFs infected with Adeno-Empty (WT) or Adeno-Cre (G12D) measured by RT-qPCR.  $n=3$  biological replicates. B) Fold change in mRNA expression of mitochondrial biogenesis genes in LSL-KrasG12D organoids infected with Adeno-Empty (WT) or Adeno-Cre (G12D) measured by RT-qPCR ( $n=3$  biological replicates). C) Fold change in mRNA expression of mitophagy mediators in LSL-KrasG12D MEFs infected with Adeno-Empty (WT) or Adeno-Cre (G12D) and measured by RT-qPCR ( $n =$  at least 3 biological replicates). Two-way ANOVA with Holm-Sidak test. D) Fold change in mRNA expression of indicated genes in LSL-KrasG12D organoids infected with Adeno-Empty (WT) or Adeno-Cre (G12D) and measured by RT-qPCR ( $n=3$  biological replicates). Two-way ANOVA with Holm-Sidak test. E) qPCR for Nix, p62, Pink1, and Park2 in pancreas samples from LSL-KrasG12D, LSL-p53R172H, Pdx1-Cre (G12D) and LSL-p53R172H, Pdx1-Cre ("WT") control mice.  $N=4$  mice per group. Two-way ANOVA with Holm-Sidak test. F) Fold change in mRNA expression of *Brn3p1* and *Acsm3* in FPC organoids treated with vehicle (Veh) or 4-OH-tamoxifen (Tam) measured by RT-qPCR ( $n=3$  biological replicates). Two-way ANOVA with Holm-Sidak test. G) Western blots for NIX level in the cytoplasmic and mitochondrial-enriched fractions of FA6 cells treated for 24 hours with control (NT), KRAS, NIX, or MAP2K2/MEK2 siRNA. H) Quantification of the relative level of mitochondrial NIX in samples from (G) taken from western blots of  $n=3$  independent experiments. One-way ANOVA with Holm-Sidak test. I) Western blot for ERK activity in FA6 cells treated with AZD6244 for 24 hours. J) Western blots for NIX in the cytoplasmic and mitochondrial-enriched fractions from FA6 cells treated as in (I).