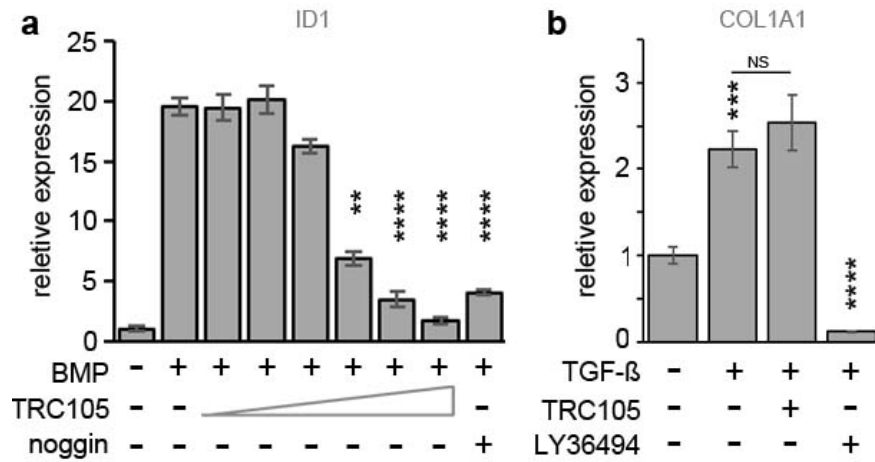
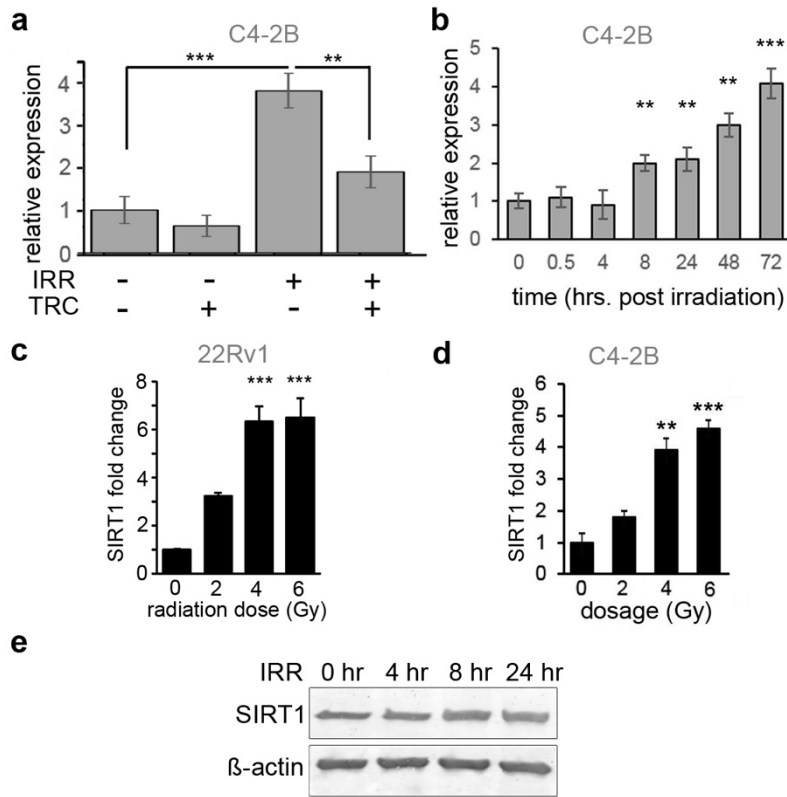


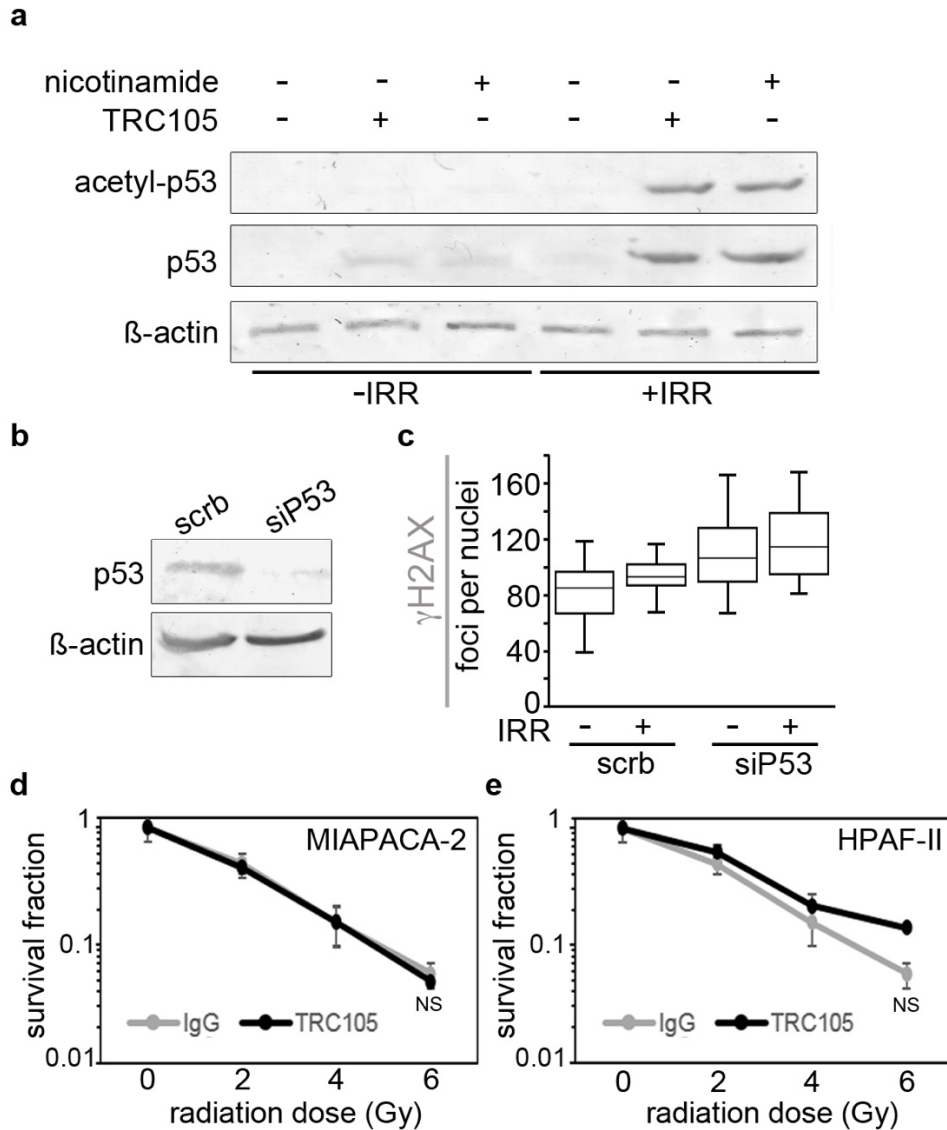
## Supplemental Figures



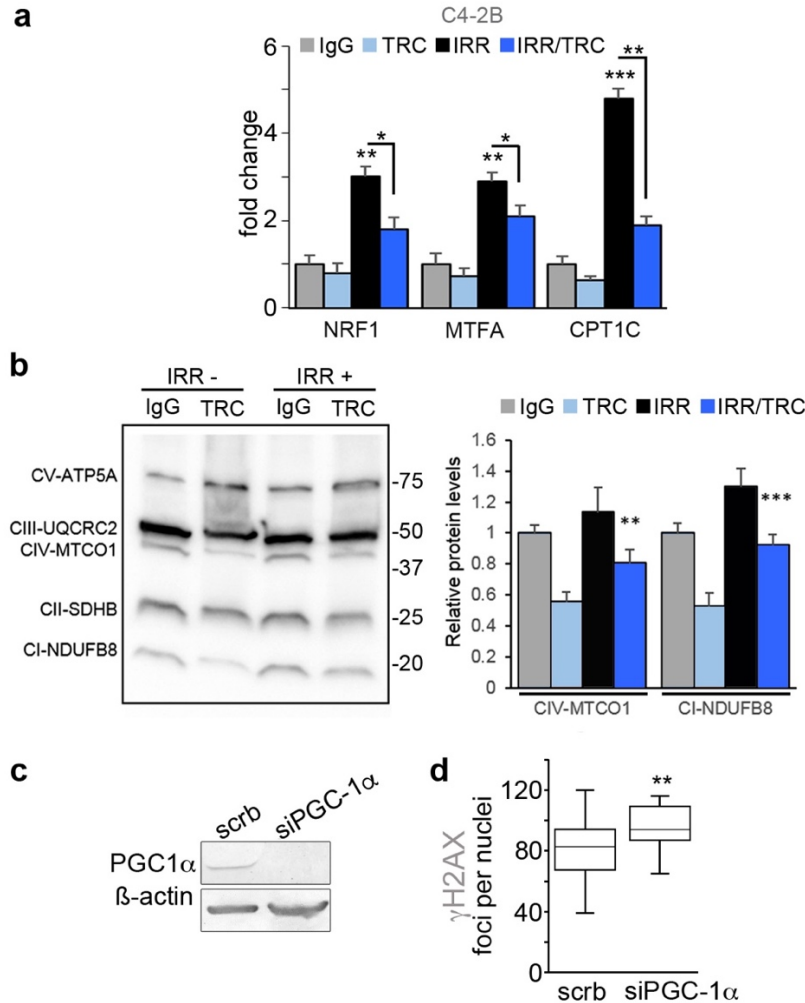
**Supplemental Figure 1. a.** ID1 mRNA expression was measured in 22Rv1 under serum free conditions with 50 ng/ml BMP4, IgG in the context of increasing doses of TRC105 (0.05, 0.1, 0.5, 1, 5, or 10  $\mu$ g/ml). **b.** Collagen 1a1 (COL1A1) mRNA expression was measured under serum free conditions with 5 ng/ml TGF- $\beta$ , TRC105 (10  $\mu$ g/ml), and/or TGF- $\beta$  antagonist (LY-36494, 10  $\mu$ M). ID1 and COL1a1 mRNA expression was normalized to GAPDH. (\*\* $p$ <0.01, \*\*\* $p$ <0.001, \*\*\*\* $p$ <0.0001, as compared to control)



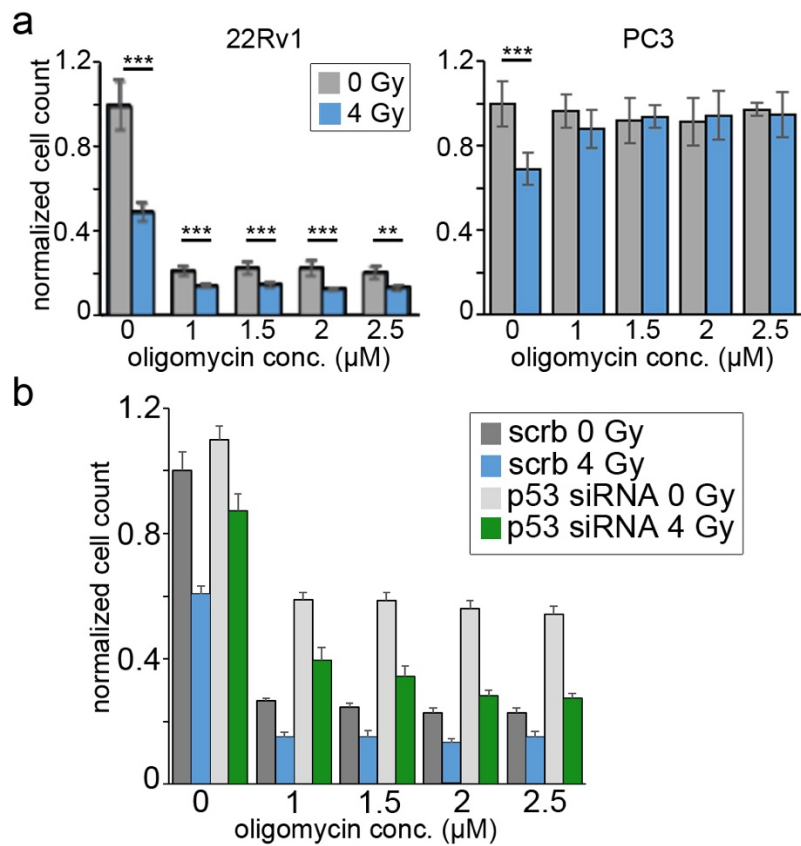
**Supplemental Figure 2:** SIRT1 mRNA expression was quantitated. **a.** C4-2B were pre-treated with IgG or TRC105 prior to irradiation with 4 Gy and compared for relative SIRT1 mRNA expression 72 hours after irradiation. **b.** C4-2B cells were irradiated (4 Gy) and SIRT1 expression measured 0, 0.5, 4, 8, 24, 48, and 72 hours post- irradiation. **c.** 22Rv1 were irradiated (0, 2, 4, or 6 Gy) and SIRT1 expression measured 72 hours post-irradiation. **d.** C4-2B were irradiated (0, 2, 4, or 6 Gy) and SIRT1 expression measured 72 hours post-irradiation. SIRT1 mRNA was normalized to GAPDH and to untreated. **e.** SIRT1 protein expression was measured at 0, 4, 8, 24 hours post 4Gy irradiation in 22Rv1 by western blot. Western blot was probed for SIRT1 and  $\beta$ -actin (\*\* $p < 0.01$ , \*\*\* $p < 0.001$  as compared to control).



**Supplemental Figure 3:** **a.** 22Rv1 cells were Western blotted 0 or 7 days following radiation in the presence of IgG, TRC105, or nicotinamide. Whole lysate was probed for total p53 and acetylated-p53 following p53 enrichment by immunoprecipitation. 22Rv1 were transfected with either Scrambled siRNA (scrb) or p53 siRNA (siP53) 48 hours prior to irradiation or collection for western blot analysis. **b.** Western blots were probed for total p53 and  $\beta$ -actin to determine efficient p53 silencing. **c.**  $\gamma$ -H2AX was immunolocalized at 4 hours post 4 Gy irradiation of scrb or siP53 22Rv1. Foci per nuclei were quantified (n = 100). **d,e.** Clonogenic survival assays were performed on two p53 mutant pancreatic cancer cell lines, MIAPACA-2 and HPAF-II with indicated doses of radiation. No significant (NS) radiation sensitization was had with TRC105 compared to IgG control.



**Supplemental Figure 4: a.** The mRNA expression of PGC-1 $\alpha$  target genes, NRF1, MTFA, and CPT1C were measured in C4-2B cells. MRNA expression was normalized to GAPDH and untreated. **b.** 22Rv1 were treated with IgG or TRC105 prior to irradiation with 4 Gy. Lysate was collected 72 hours post-irradiation for Western blot. Blots were probed for a cocktail of mitochondrial complex proteins. Protein levels of MTCO1 of complex-IV and NDUFB8 of complex-I in 3 independent experiments were normalized to Ponceau S. MTCO1 and NDUFB8 were significantly lower in 4 Gy with TRC105 compared to radiation alone. 22Rv1 were transfected with either scrambled siRNA (scr) or PGC-1 $\alpha$  siRNA (siPGC-1 $\alpha$ ) 48 hours prior to radiation treatment or collection for western blot analysis. **c.** Western blots were probed for total PGC-1 $\alpha$  and  $\beta$ -actin to determine efficient PGC-1 $\alpha$  knockdown. **d.**  $\gamma$ -H2AX was immunolocalized in scr or siPGC-1 $\alpha$  22Rv1 cells 4 hours after 4 Gy irradiation. Foci per nuclei were quantified (n = 100). (\*p<0.05, \*\*p<0.01, \*\*\*p<0.001).



**Supplemental Figure 5. a.** The role of ATP depletion on radiation sensitivity was tested by treating 22Rv1 and PC3 cells with indicated doses of ATPase inhibitor, oligomycin and exposed to 4 Gy irradiation. Cell counts were performed 72 hours following irradiation. (\*\* $p < 0.01$ , \*\*\* $p < 0.001$ ). **b.** Scrambled and p53 siRNA transfected 22Rv1 were treated with indicated doses of oligomycin and exposed to 4Gy irradiation. Cell counts were performed 72 hours following irradiation.

**Supplemental Table 1. Primer Sequences**

Gene	Sequence
ID1 Forward	5'-AAT CAT GAA AGT CGC CAG TG-3'
ID1 Reverse	5'-ATG TCG TAG AGC AGC ACG TTT-3'
COL1A1 Forward	TCTGCGACAACGGCAAGGTG
COL1A1 Reverse	GACGCCGGTGGTTTCTTGGT
SIRT1 Forward	5'-TGC TGG CCT AAT AGA GTG GCA AAG-3'
SIRT1 Reverse	5'- GGC ATG TCC CAC TAT CAC TGT-3'
NRF1 Forward	5'-CAG CAG GTC CAT GTG GCT ACT-3'
NRF1 Reverse	5'-GCC GTT TCC GTT TCT TTC C-3'
MTFA Forward	5'-GAT GCT TAT AGG GCG GAG TGG-3'
MTFA Reverse	5'-GCT GAA CGA GGT CTT TTT GGT-3'
CPT1C Forward	5'-TTT CTG GGT GAC GGT GAT CTC-3'
CPT1C Reverse	5'-CAT ATG TCC AAT CCC AGT GCA A-3'
GAPDH Forward	5'-CAT GAG AAG TAT GAC AAC AGC CT-3'
GAPDH Reverse	5'-AGT CCT TCC ACG ATA CCA AAG T-3'
MT-CO2 Forward	5'-CCT GCG ACT CCT TGA CGT TG-3'
MT-CO2 Reverse	5'-AGC GGT GAA AGT GGT TTG GTT-3'
ACTB Forward	5'-TCA CCC ACA CTG TGC CCA TCT ACG A-3'
ACTB Reverse	5'-CAG CGG AAC CGC TCA TTG CCA ATG G-3'
BMP2 Forward	5'-ATGGATTCGTGGTGGGAAGTG-3'
BMP2 Reverse	5'-GTGGAGTTCAGATGATCAGC-3'
BMP4 Forward	5'-AGCATGTCAGGATTAGCCGA-3'
BMP4 Reverse	5'-TGGAGATGGCACTCAGTTCA-3'
BMP6 Forward	5'-CAGCCTGCAGGAAGCATGAG-3'
BMP6 Reverse	5'-CAAAGTAAAGAACCGAGATG-3'
BMP7 Forward	5'-TGGAACATGACAAGGAATTCT-3'
BMP7 Reverse	5'-CATCCAGCGTCTCCACCGAGA-3'
BMP9 Forward	5'-AGAACGTGAAGGTGGATTTCC-3'
BMP9 Reverse	5'-CGCACAATGTTGGACGCTG-3'
TGFb1 Forward	5'-CCCAGCATCTGCAAAGCTC-3'
TGFb1 Reverse	5'-GTCAATGTACAGCTGCCGCA-3'
TGFb2 Forward	5'-CCGCATCTCCTGCTAATGTTG-3'
TGFb2 Reverse	5'-AATAGGCGGCATCCAAAGC-3'
Activin A Forward	5'-TGGGCAAGAAGAAGAAGAAA-3'
Activin A Reverse	5'-CACTCACCCTCGCAGTAGTT-3'
LRG1 Forward	5'-GTTGGAGACCTTGCCACCT-3'
LRG1 Reverse	5'-GCTTGTTGCCGTTTCAGGA-3'