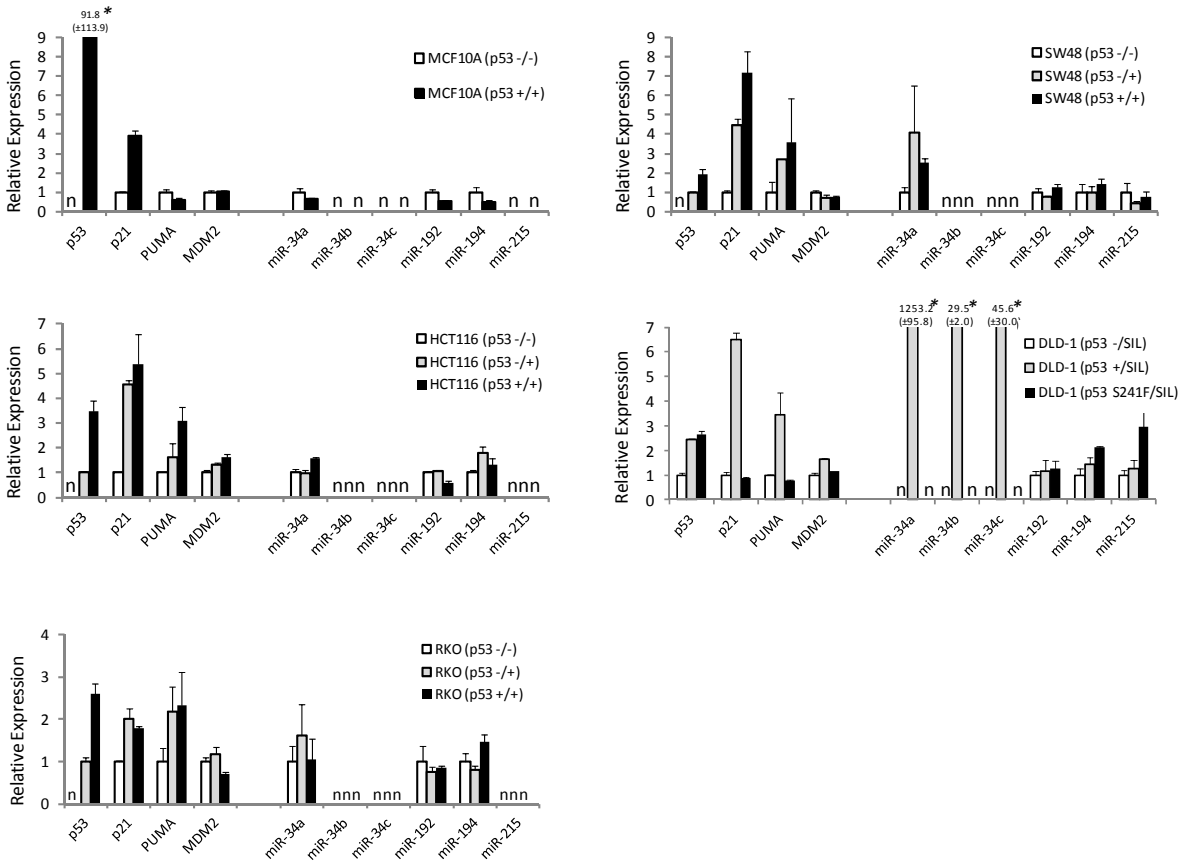
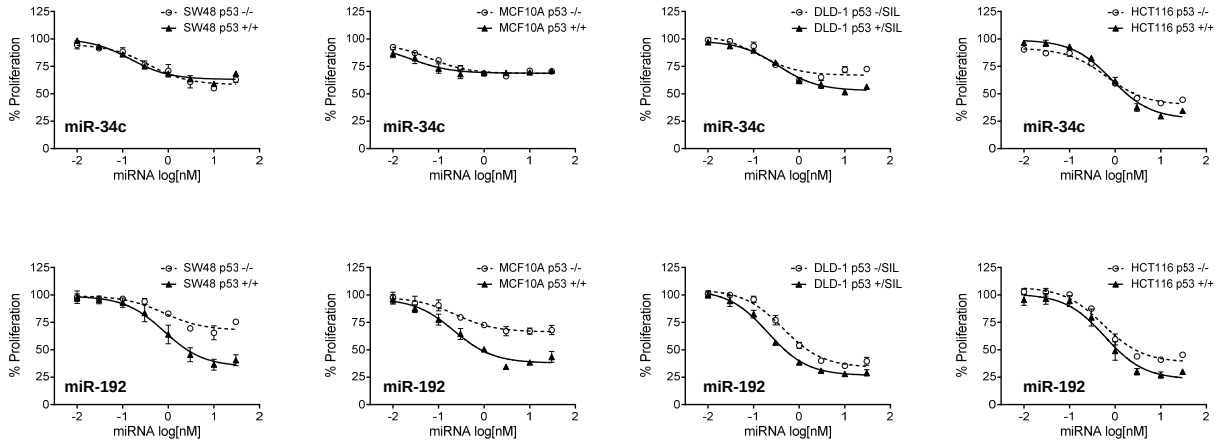
Supplementary Table 1: *TP53* genotypes of isogenic cancer cell lines

Cell Line	*TP53* Genotype	Allele 1	Allele 2	Other Mutations*
SW48 +/+	+/+	WT	WT	*CTNNB1, EGFR, FBXW7*
SW48 +/-	+/-	WT	Inactivated	
SW48 -/-	-/-	Inactivated	Inactivated	
HCT116 +/+	+/+	WT	WT	*CTNNB1, CDKN2A, KRAS, MLH1, PIK3CA*
HCT116 +/-	+/-	WT	Inactivated	
HCT116 -/-	-/-	Inactivated	Inactivated	
RKO +/+	+/+	WT	WT	*BRAF, NF1, PIK3CA*
RKO +/-	+/-	WT	Inactivated	
RKO -/-	-/-	Inactivated	Inactivated	
DLD-1 S241/SIL	S241F/SIL	S241F	Silent	not documented
DLD-1 +/SIL	+/SIL	WT	Silent	
DLD-1 -/SIL	-/SIL	Inactivated	Silent	
MCF10A +/+	+/+	WT	WT	not documented
MCF10A -/-	-/-	Inactivated	Inactivated	

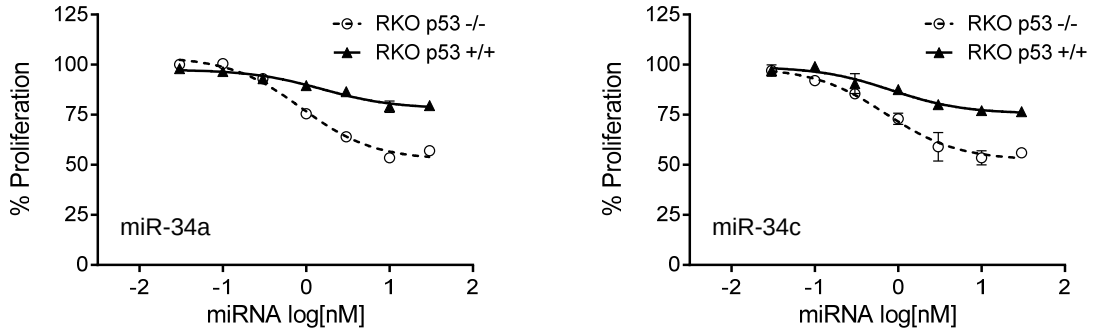
* as reported by the Catalogue of Somatic Mutations in Cancer (COSMIC, www.sanger.ac.uk) database



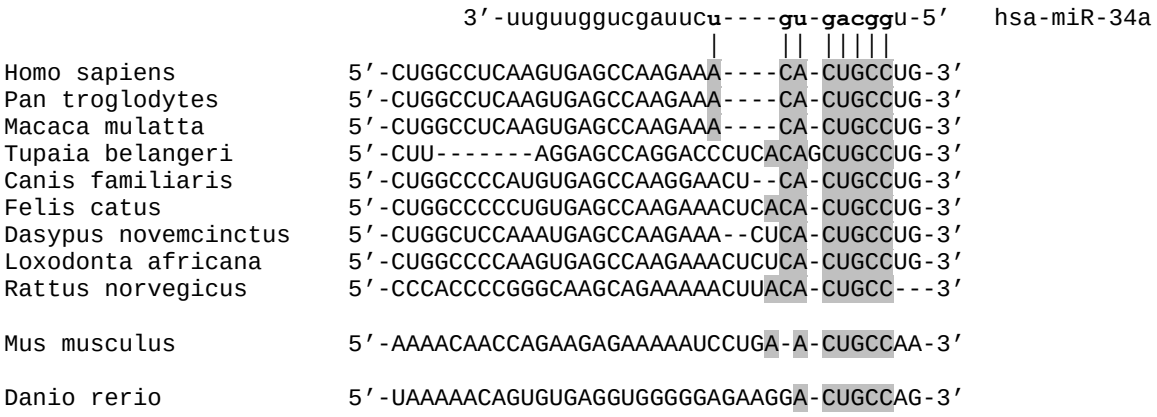
Supplementary Figure 1:
Induction of TP53 genes by etoposide. Isogenic cancer cells were incubated in the presence of 10 µM etoposide for 28 hours. Total RNA was harvested and used in qRT-PCR to measure endogenous mRNA and miRNA levels. mRNA levels of *TP53* are normalized to those in *TP53*$^{+/-}$ cells (SW48, HCT116, RKO) or TP53$^{-/-}$ cells (MCF10A; expression = 1). Data from DLD-1 cells are normalized to DLD-1^{par} cells. All other data are normalized to expression levels in *TP53*-deficient cells (-/-; relative expression = 1). Averages and standard deviations are shown. n, not detected; *, data are normalized to a standardized PCR threshold due to absence in reference cells.



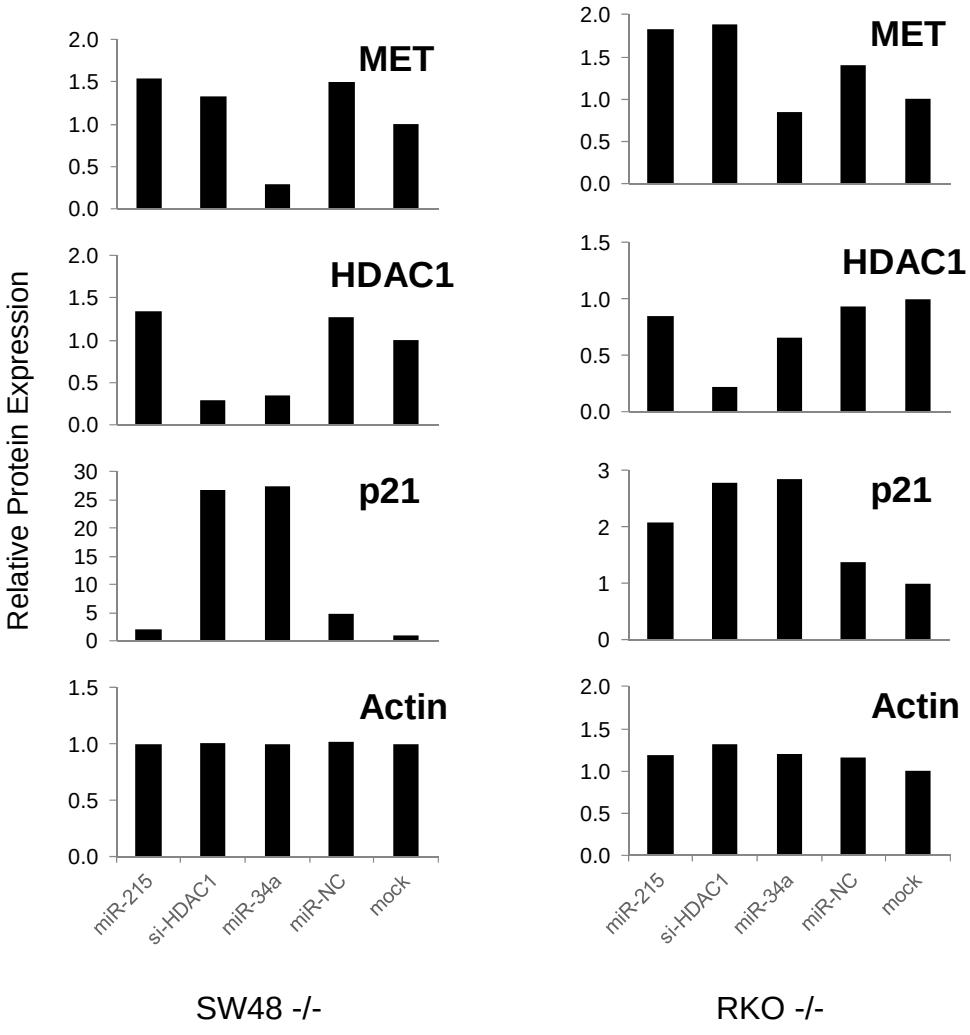
Supplementary Figure 2:
Dose-dependent effects of miR-34c and miR-192 in cancer cells with or without functional *TP53*. Cells were transfected with miRNA mimics in a serial dilution in 96-well plates. After 3 days, cellular proliferation was determined by AlamarBlue. Averages and standard deviations are shown.



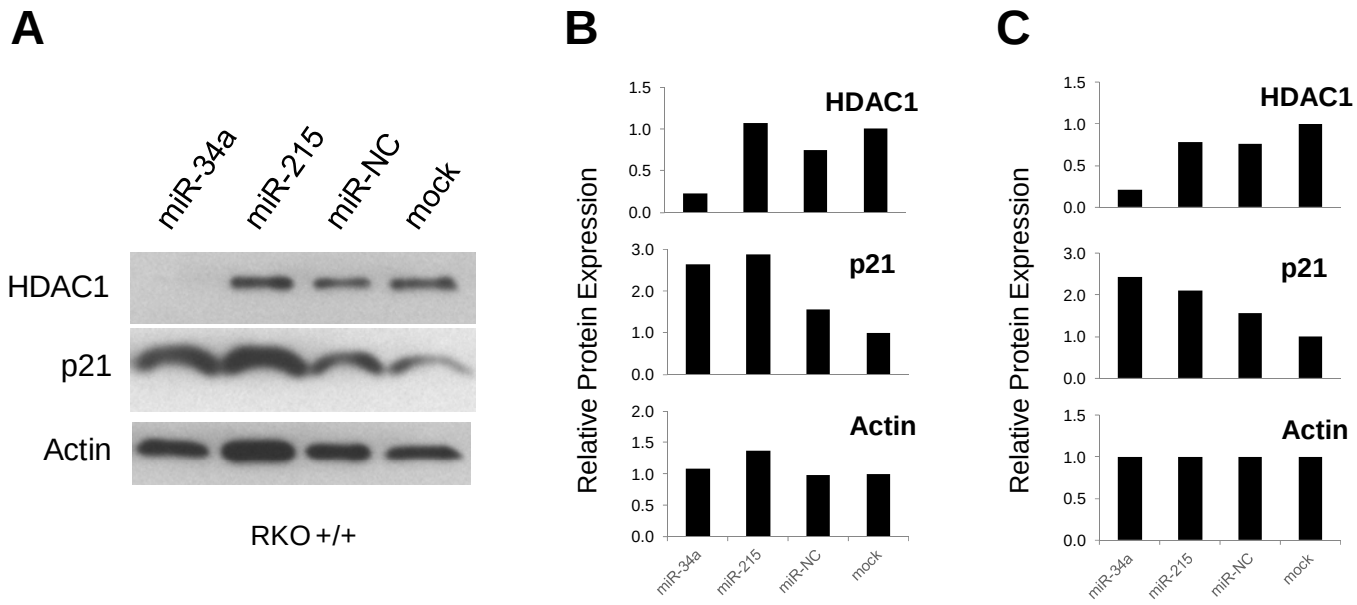
Supplementary Figure 3:
Dose-dependent effects of miR-34a and miR-34c in isogenic RKO cells. Cells were transfected with miRNA mimics in a serial dilution in 96-well plates. After 3 days, cellular proliferation was determined by AlamarBlue. Averages are shown. Standard deviation bars are included in the graphs but are occasionally too small to be visible.



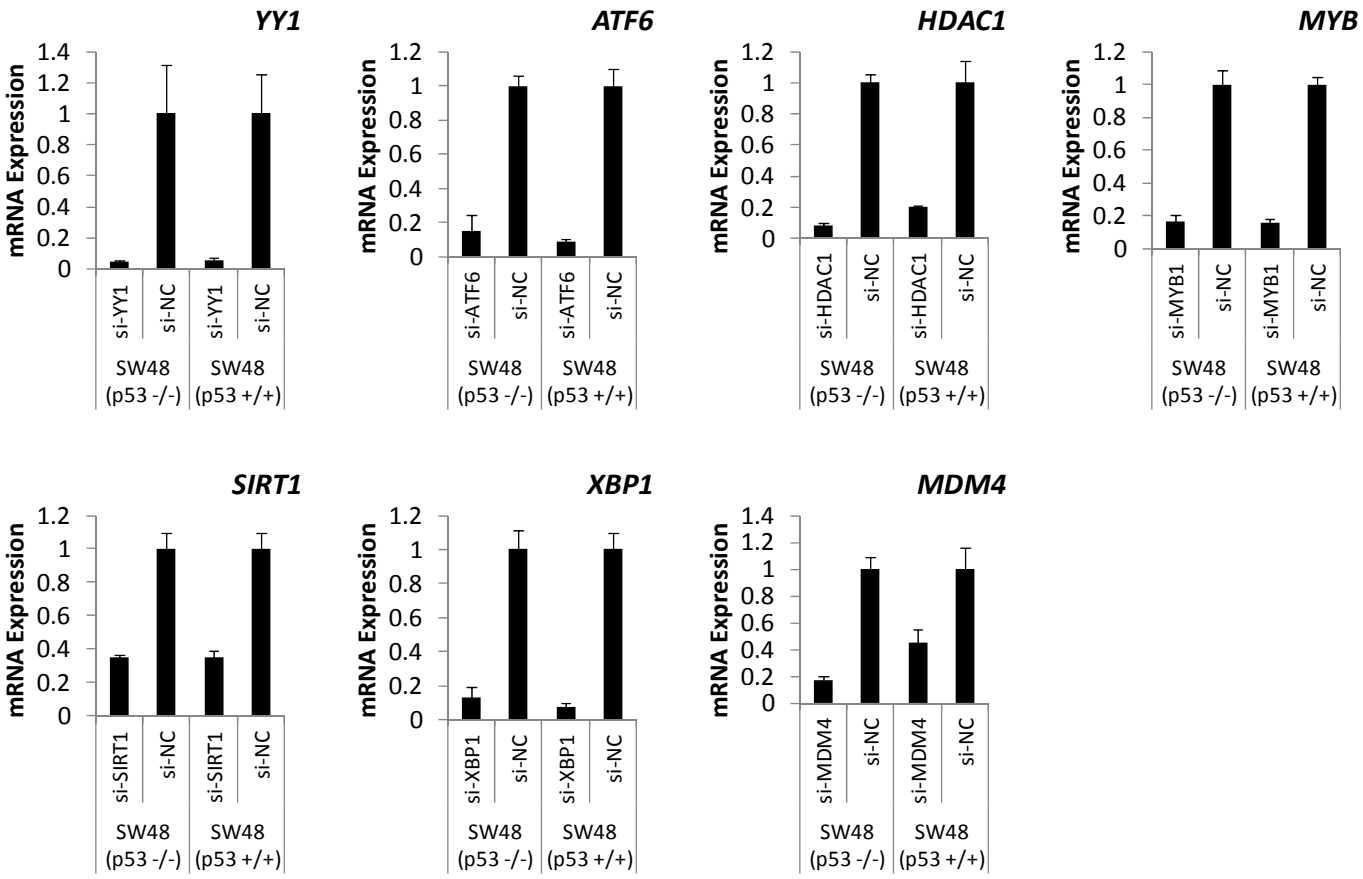
Supplementary Figure 4:
Conservation of miR-34a binding sites in the HDAC1 3'-UTR across vertebrates. Base pairing of miR-34a with *HDAC1* 3'UTR sequences are shown. Alignments were created using the TargetScan and miRanda algorithms. Lower case, miR-34a residues; upper case, mRNA residues; grey, bases that align to miR-34a seed sequence; bold, miR-34a seed sequence.



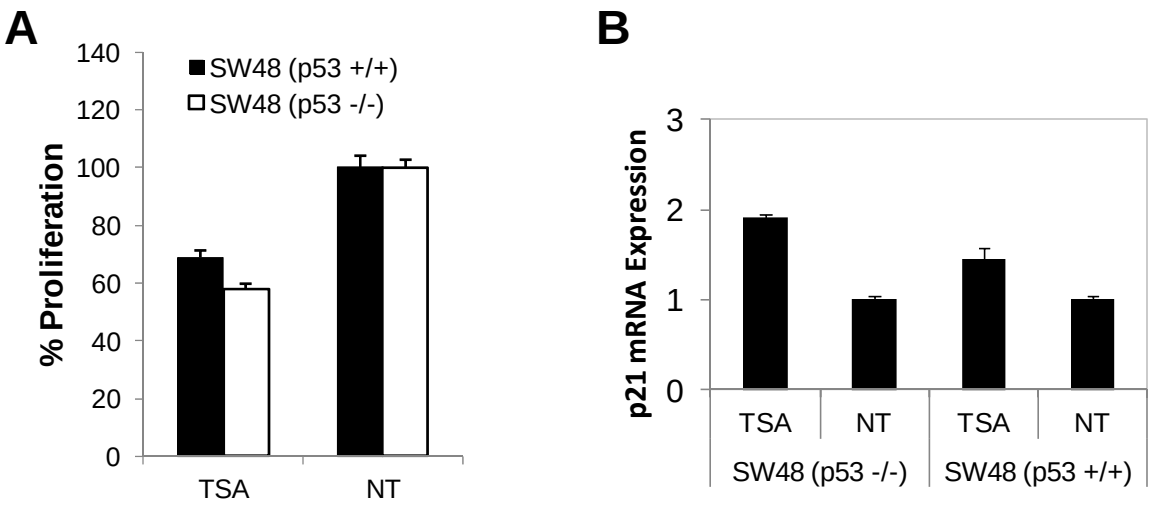
Supplementary Figure 5:
Quantification of Western data shown in Figure 4A using the AlphaImager EC instrument from Cell Biosciences Inc. Data are normalized to those from mock-transfected cells (expression = 1).



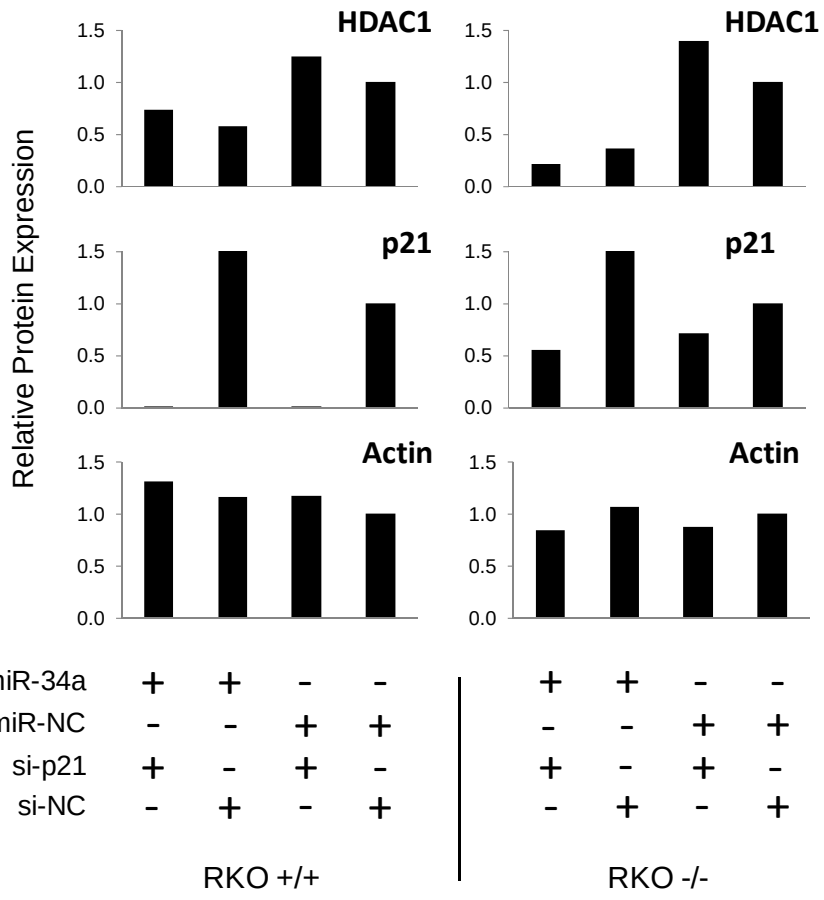
Supplementary Figure 6:
miR-34a-induced repression of HDAC1 and induction of $p21^{CIP1/WAF1}$ in TP53-positive cells. (A) Cells lysates from cells were prepared 3 days after transfection with miRNA mimics. Lysates were probed by Western analysis. (B) Western data shown in A quantified by the AlphaImager EC instrument from Cell Biosciences Inc. Data are normalized to those from mock-transfected cells (expression = 1). (C) Quantification of Western data normalized to the loading control Actin.



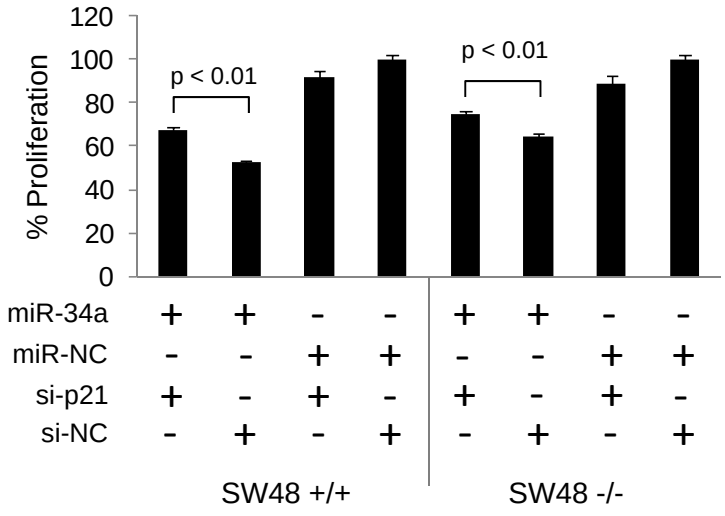
Supplementary Figure 7:
Endogenous mRNA expression levels in isogenic SW48 cells transiently transfected with siRNAs. Expression levels are normalized to those of cells transfected with negative control siRNA (si-NC). Averages and standard deviations of triplicate experiments are shown. mRNA levels of *MYCN*, *MYCT1* and *SNAI2* were not detectable in any of the isogenic SW48 cell lines used.



Supplementary Figure 8:
Effects of TSA on isogenic cancer cells. (A) TSA-treatment equally inhibits cellular proliferation of $SW48^{-/-}$ and $SW48^{+/+}$ cells. Cells were incubated with 400 nM TSA. An assessment of proliferation and RNA isolation was carried out 24 hrs thereafter. Values are normalized to non-treated cells (NT). (B) qRT-PCR analysis measuring $p21^{CIP1/WAF1}$ mRNA levels using RNA samples from cells treated with TSA.



Supplementary Figure 9:
Quantification of Western data shown in Figure 5A using the AlphaImager EC from Cell Biosciences Inc. Data are normalized to those from mock-transfected cells (expression = 1).



Supplementary Figure 10:
Depletion of p21 interferes with miR-34a-induced inhibition of cell proliferation in SW48 cells. miRNA mimics and siRNAs were transiently transfected into isogenic SW48 as cells as shown in the graph. Proliferation was assessed by Alamar Blue and normalized to cells transfected with negative control (100%). Averages and standard deviations of triplicates are shown. P values were derived from a 2-tailed Student's t test.