

Supplemental figure legends

Figure S1. Expression of potential dual-targeting miRNAs in human cancers. (A) Table listing candidate microRNAs which are upregulated in prostate (GSE21036), colon (GSE18392) and/or kidney cancers (GSE37989). **(B,C)** Expression of miRs-518c*, 584 and 638 in colon (B) and kidney (C) cancers.

Figure S2. miR-638 directly targets PTEN and p53. (A) List of the predicted MREs on the PTEN and p53 mRNAs. **(B)** Luciferase validation assays demonstrating the effect of miR-638 overexpression on its predicted PTEN and p53 MREs cloned in the luciferase 3'UTR in PC3, HCT116 and U2OS cells. **(C)** Luciferase validation assays demonstrating the effect of miR-638 overexpression on its predicted PTEN and p53 MREs cloned in the respective locations of the luciferase transcript in PC3 cells. 5'UTR MREs were placed in the luciferase 5'UTR and CDS MREs were placed just upstream of the luciferase stop codon. **(D)** Luciferase validation assays demonstrating the effect of miR-638 overexpression on the respective wild-type and MRE-mutant luciferase constructs in PC3 cells. Site-directed mutagenesis was performed to mutate the seed regions of the PTEN C1, 3'1, p53 C1 and 3'1 MREs in the corresponding psicheck2 constructs containing the wild-type full-length PTEN CDS, 3'UTR, p53 CDS and 3'UTR fragments respectively. (B-D) The miR-638 reverse complement (638RC) is shown as a positive control. Mean \pm SD; $n \geq 4$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Figure S3. Overexpression of miRs-638 and 518c* promotes tumorigenesis. (A) Wound healing assay demonstrating the effect of miR-518c* or 638 overexpression on migration of U2OS cells. **(B-C)** Quantitation of the transwell migration (B) and invasion (C) assays shown in Figures 3A and B respectively. **(D-E)** Quantitation of the average number (D) and size (E) of the soft agar colonies shown in Figure 3D. **(F)** Effect of miR-638 overexpression on HCT116 xenograft tumor formation in nude mice. **(G)** Expression levels of miR-638 in HCT116 and U2OS cells transfected with various amounts of miR-638 mimic.

Figure S4. miR-638 is part of the oncogenic DNM2 locus. (A) Expression levels of endogenous miR-638 in a panel of cell lines expressing wild-type PTEN, p53 and BRCA1. **(B)** Genomic alterations of the miR-638 locus in various human cancers (data generated by the TCGA Research Network: <http://cancergenome.nih.gov/>). **(C)** Expression of DNM2 transcript in various publicly available ovarian cancer microarray datasets. **(D)** Effect of miR-638 (left panel) or DNM2 (right panel) genomic alterations on ovarian cancer survival (data generated by the TCGA Research Network: <http://cancergenome.nih.gov/>).

Supplemental table legend

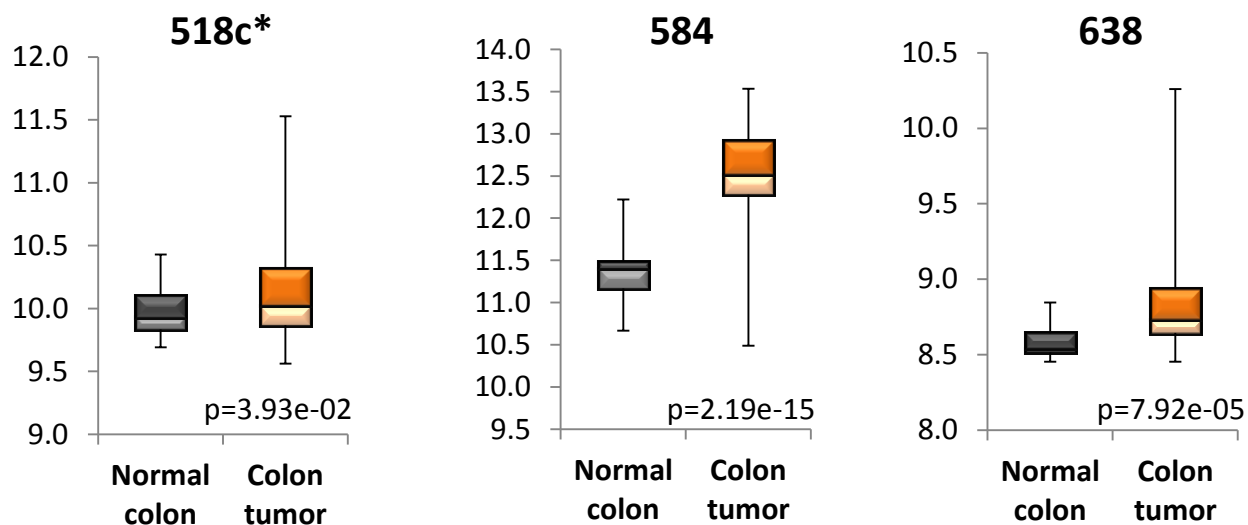
Table S1. List of microRNAs predicted to target the PTEN and/or p53 transcripts.

Figure S1, Related to Figure 1

A

	Prostate GSE21036	Colon GSE18392	Kidney GSE37989
miR-30c-1*	x		
miR-139-3p	x		
miR-149*	x		
miR-185	x		x
miR-193b*	x		
miR-518c*	x	x	x
miR-584	x	x	x
miR-638	x	x	x
miR-663	x		x
miR-760	x		
miR-769-3p	x		x
miR-939	x		

B



C

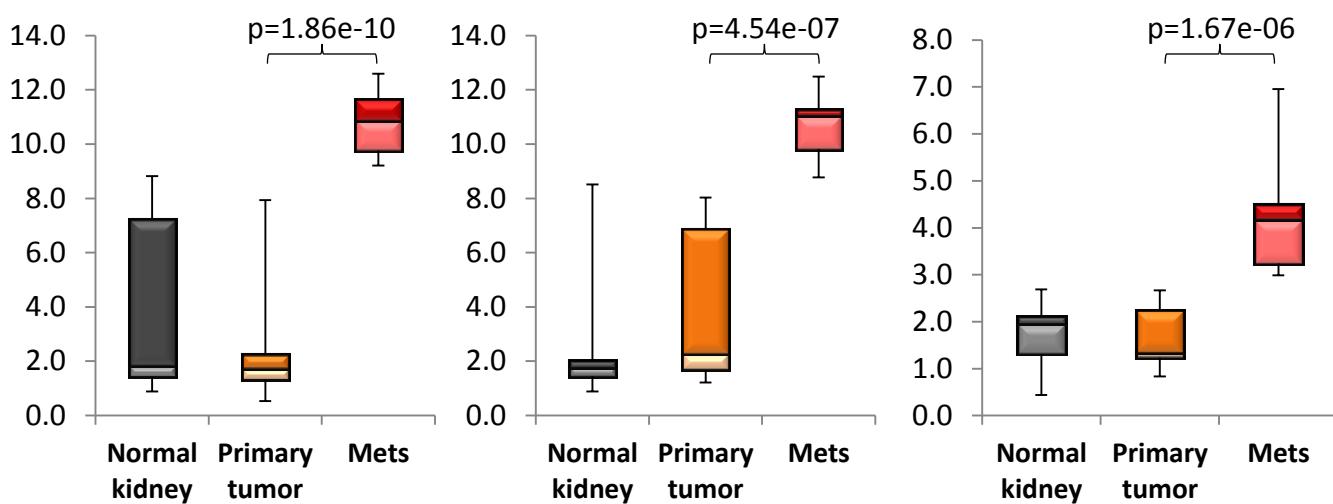
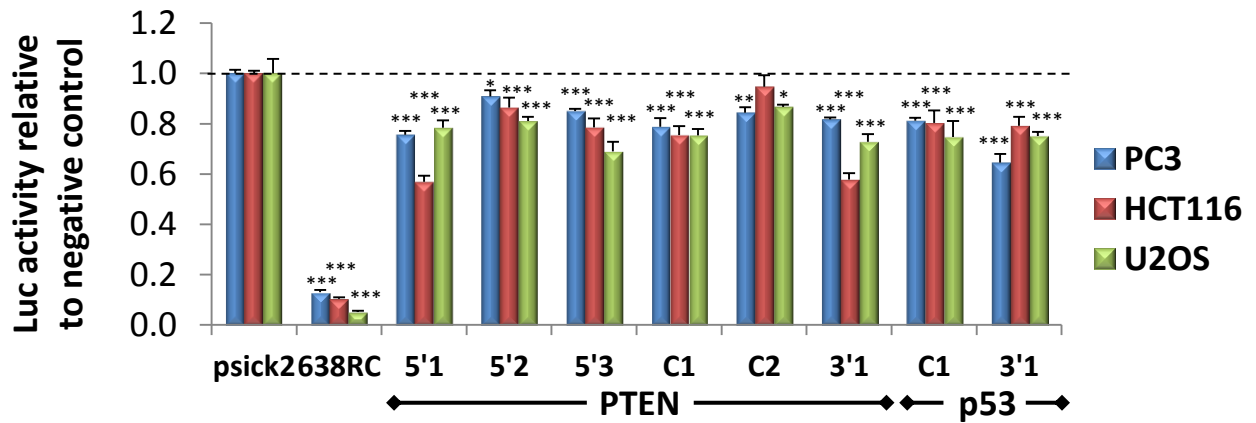


Figure S2, related to Figure 2

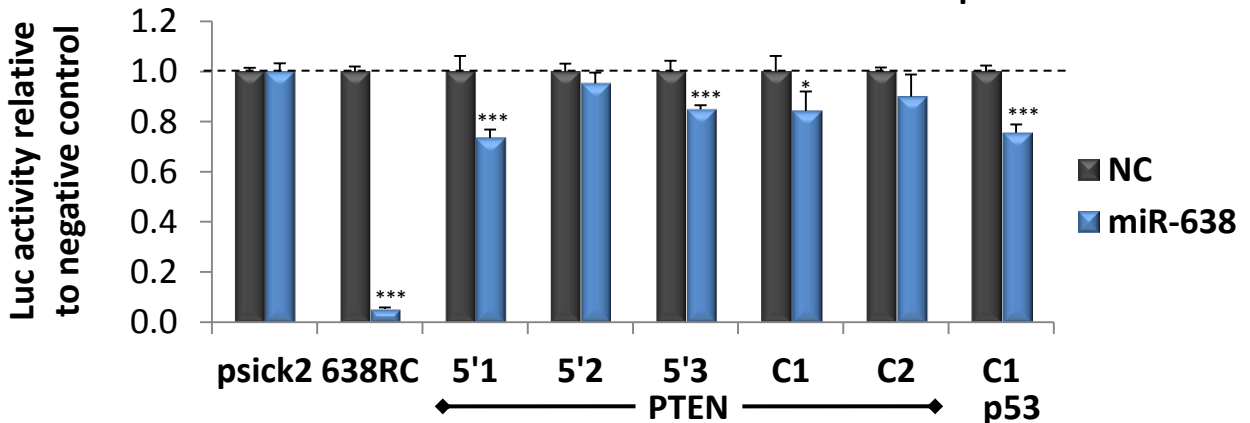
A

MiRNA	Transcript	Location	MRE name	Offset	MRE sequence	Folding energy	Paired bases
518c*	PTEN	5'UTR	5'1	597 to 619	TCCAGGGCTGGGAACGCCGGAGA	-27.3	14
		CDS	C1	1494 to 1516	TATGGGAAGTAAGGACCAGAGA	-27.8	14
	P53	CDS	C2	1525 to 1547	GAGTAACTATCCCAGTCAGAGG	-28.4	15
		5'UTR	5'1	87 to 109	AGGTAGCTGCTGGGCTCCGGGGA	-33.6	18
584	PTEN	CDS	C1	1031 to 1053	TGGGAGAGACCGCGCACAGAGG	-26.6	15
		5'UTR	5'1	196 to 217	CTCTCGGAAGCTGCAGCCATGA	-27.1	16
	P53	CDS	C1	1534 to 1555	TTCCAGTCAGAGGCGCTATGT	-27.5	15
		5'UTR	5'1	180 to 201	GCCTCCGGGTCACTGCCATGG	-30.1	16
638	PTEN	CDS	C1	1318 to 1339	GTCAGTCTACCTCCGCCATAA	-29.5	14
		5'UTR	5'1	605 to 629	TGGGAACGCCGGAGAGTTGGTCTCT	-31.9	17
		5'UTR	5'2	872 to 896	CAGCCATTACCCGGCTGCGGTCCAG	-45.6	19
		5'UTR	5'3	973 to 997	GCCACCAGCAGCTTCTGCCATCTCT	-38.2	18
		CDS	C1	1661 to 1685	TTGCAATCCTCAGTTTGTGGTCTGC	-27.3	18
		CDS	C2	2169 to 2193	TCTGACACCACTGACTCTGATCCAG	-29.5	15
	P53	3'UTR	3'1	4778 to 4802	GAAATGCATTCTGTAGGTAACTCT	-28.8	15
		CDS	C1	198 to 222	ATGGAGGAGCCGAGTCAGATCCTA	-34.4	17
		3'UTR	3'1	1435 to 1459	TGCCATTTGGGTTTGGGTCTTT	-28.7	20

B



C



D

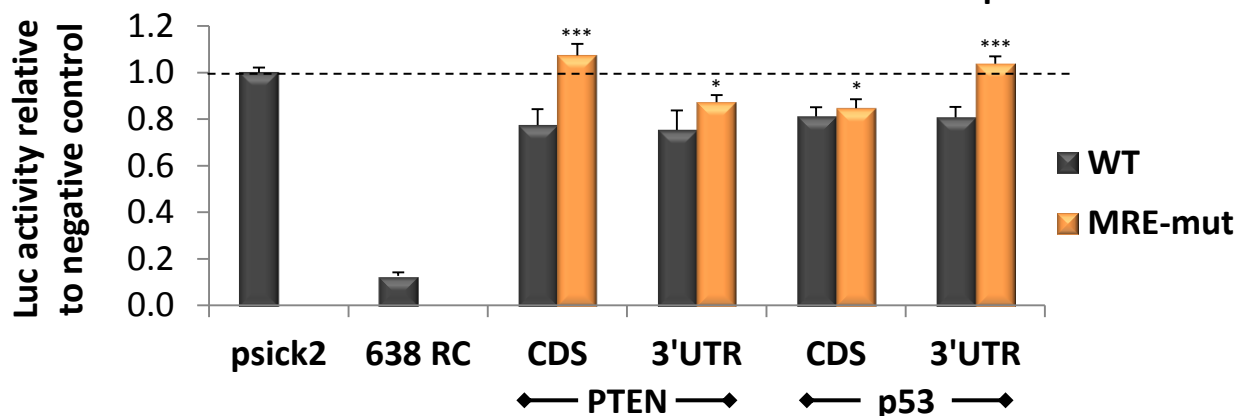


Figure S3, related to Figure 3

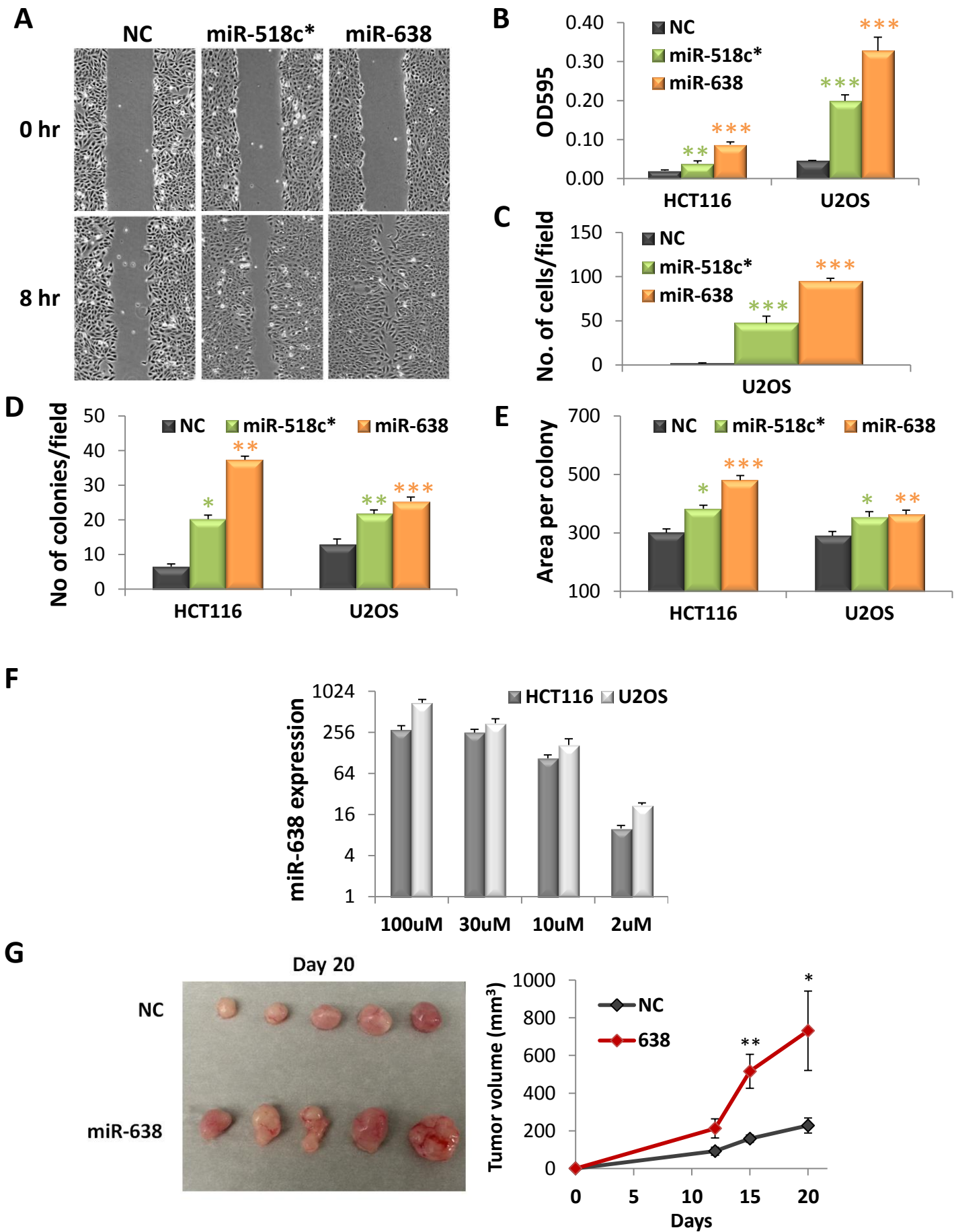
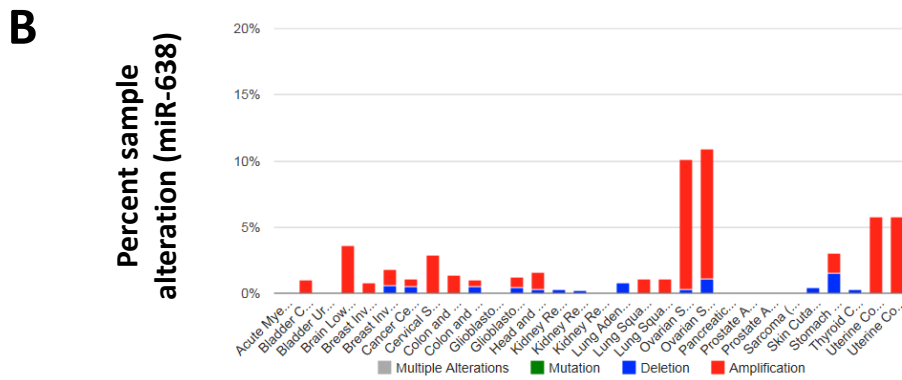
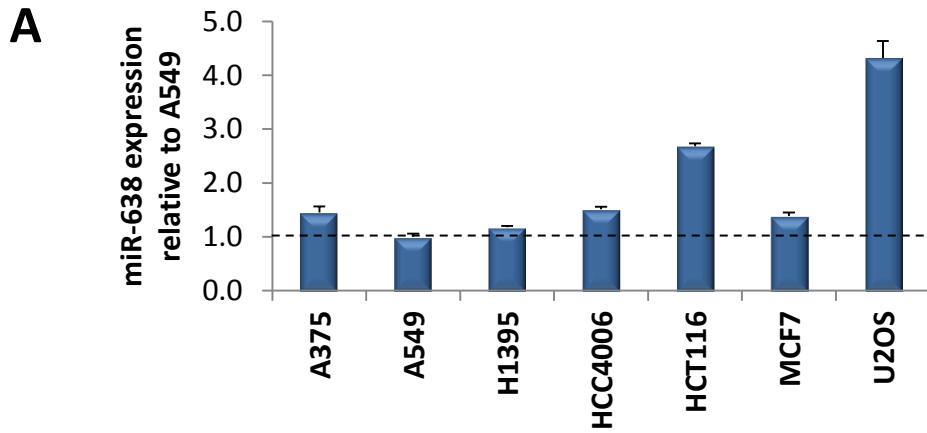


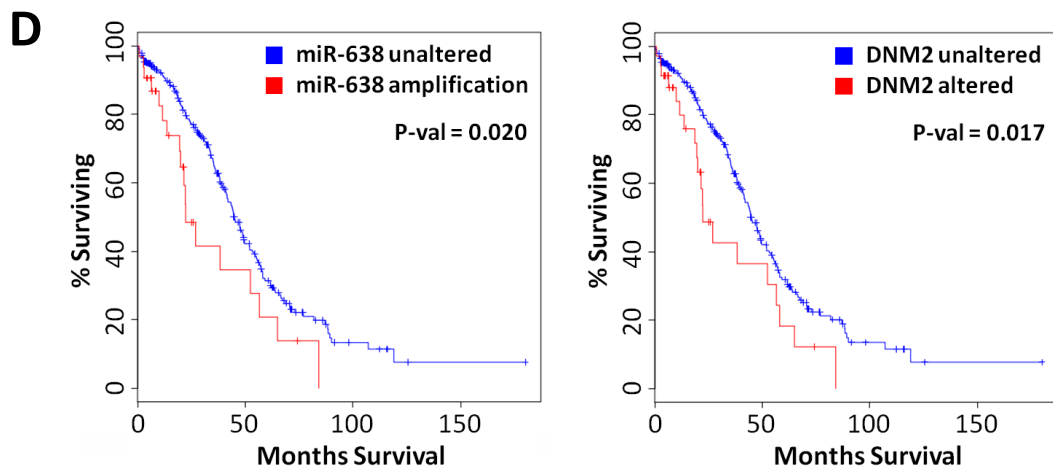
Figure S4, related to Figure 5



C

Ovarian cancer

DNM2 Gene rank	Fold change	P-val	Reference
8 (1%)	1.973	1.86e-5	Adib et al, 2004
72 (2%)	36.067	4.84e-9	Welsh et al, 2001
986 (6%)	1.513	0.008	Lu et al, 2004
1812 (15%)	1.632	2.35e-6	Bonome et al, 2008



**Table S1,
related to
Figure 1**

	PTEN	p53
let-7a		x
let-7b	x	x
let-7e	x	x
let-7f	x	
let-7i*	x	
miR-9	x	x
miR-10b*	x	
miR-17*	x	
miR-20b*	x	
miR-23a*	x	x
miR-23b*	x	
miR-24	x	x
miR-24-2*		x
miR-27a*	x	
miR-29b-1*	x	
miR-29b-2*	x	x
miR-30a		x
miR-30a*	x	x
miR-30c-1*	x	x
miR-30c-2*		x
miR-30d*		x
miR-33a	x	
miR-34a	x	x
miR-92a-1*	x	
miR-92a-2*	x	x
miR-92b*		x
miR-93*	x	
miR-99b*	x	
miR-103-2*		x
miR-103-as		x
miR-125a-3p	x	
miR-125b-1*	x	
miR-127-3p	x	x
miR-129-5p	x	x
miR-130a		x
miR-130b		x
miR-130b*	x	x
miR-138	x	x
miR-139-3p	x	x
miR-140-5p		x
miR-141*		x
miR-146b-3p		x
miR-149	x	
miR-149*	x	x
miR-150		x
miR-151-3p		x
miR-151-5p	x	x
miR-182	x	
miR-182*	x	
miR-185	x	x
miR-185*	x	x
miR-188-5p		x
miR-191*	x	
miR-193a-5p		x
miR-193b*	x	x
miR-198		x
miR-200a*		x
miR-200c*	x	
miR-202		x
miR-204	x	x
miR-205	x	x
miR-206	x	

	PTEN	p53
miR-211	x	x
miR-221	x	
miR-296-3p	x	
miR-298	x	x
miR-232b-5p		x
miR-302d*	x	
miR-323-5p	x	
miR-324-3p	x	
miR-326	x	x
miR-330-5p	x	x
miR-342-5p	x	
miR-346	x	
miR-365*		x
miR-367*	x	
miR-370	x	
miR-373	x	
miR-375		x
miR-377*	x	
miR-381	x	
miR-382	x	x
miR-409-3p	x	
miR-423-3p		x
miR-423-5p	x	
miR-431*	x	x
miR-432	x	x
miR-432*	x	
miR-448		x
miR-449a	x	
miR-449b		x
miR-449c		x
miR-453	x	
miR-486-3p		x
miR-491-5p		x
miR-500		x
miR-500*		x
miR-501-5p	x	x
miR-502-5p	x	x
miR-503		x
miR-504		x
miR-505*	x	
miR-509-3-5p	x	
miR-511		x
miR-512-3p	x	
miR-516a-5p		x
miR-517*		x
miR-518c		x
miR-518c*	x	x
miR-518e*	x	
miR-519a*	x	
miR-519b-5p	x	
miR-519c-5p	x	
miR-520-5p	x	
miR-522*	x	
miR-523*	x	
miR-541		x
miR-542-5p		x
miR-550*		x
miR-552	x	
miR-557	x	
miR-571	x	
miR-574-5p	x	
miR-578	x	

	PTEN	p53
miR-584	x	x
miR-587		x
miR-588		x
miR-593*		x
miR-595		x
miR-596	x	x
miR-601	x	
miR-602	x	
miR-604	x	x
miR-608	x	x
miR-609		x
miR-612	x	x
miR-615-5p	x	x
miR-616	x	
miR-616*		x
miR-619	x	x
miR-623	x	
miR-625		x
miR-629*	x	
miR-630		x
miR-631		x
miR-632	x	
miR-637	x	x
miR-638	x	x
miR-639	x	x
miR-645		x
miR-647	x	
miR-648	x	
miR-650	x	
miR-654-5p		x
miR-657	x	x
miR-658		x
miR-659	x	
miR-661		x
miR-663	x	x
miR-663b	x	x
miR-665		x
miR-671-3p	x	
miR-671-5p	x	
miR-708		x
miR-744		x
miR-744*	x	
miR-759		x
miR-760	x	x
miR-761		x
miR-762		x
miR-765	x	
miR-767-3p	x	x
miR-769-3p	x	x
miR-769-5p		x
miR-770-5p		x
miR-875-3p	x	x
miR-885-3p	x	
miR-886-3p	x	
miR-886-5p	x	
miR-920	x	x
miR-922		x
miR-933		x
miR-939	x	x
miR-942	x	