Supplementary Matherials and Methods

Plasmids and RNA Transfection

Reporter vector psi-CHEK2-3'UTR-RAD17 was generated by cloning 702 bp from the *RAD17*-3'UTR region in the XhoI and NotI sites of psi-CHEK2^{TM} (Promega, Madison, WI, USA). Primers used for the amplifications are listed in the Supplementary Table S5. Reporter vector pMirTarget-3'UTR-BRCA1 was purchased by OriGene Technologies, Inc. (Catalog No. SC214395; Accession No. NM_007294). Plasmids are transduced in the cells with Lipofectamine 2000 following the manufacturer's instructions (Invitrogen, Carlsbad, CA, USA). *RAD17* and *BRCA1* 3'UTR mutants were made with the QuikChange site-directed mutagenesis kit (Stratagene) using the primers listed in the Supplementary Table S5.

Synthetic mir-205-5p mimic (n° M-00202) and mimic negative control N1 (n° K-01000) were purchased by Riboxx Life Sciences. LNA miR-205-5p inhibitor (n° YI04101508) and LNA negative control A (n° YI00199006) were purchased by Exiqon-Qiagen. A total of 1×10^6 cells were transfected at 200 pmol/µl oligos concentrations. RNAs were transduced in the cells using RNAiMAX following the manufacturer's instructions (Invitrogen, Carlsbad, CA, USA).

3D cell cultures were transfected with LNA oligos after the matrix cross-linking, using RNAiMAX following the manufacturer's instructions (Invitrogen, Carlsbad, CA, USA). The culture medium was replaced after between 48h from transfection.

Cell extracts, western and dot blotting

Cells derived from 2D and 3D cultures were homogenized in a lysis buffer composed by 50 mM Hepes pH 7.5, 5 mM EDTA pH 8.0, 10 mM MgCl2, 150 mM NaCl, 50 mM NaF, 20 mM β-glicerophosphate, 0.5% NP40, 0.1 mM sodium orthovanadate, 1 mM PMSF, 1 mM DTT and protease and phosphatase inhibitors. Extracts were sonicated for 20 sec and clarified by centrifugation to remove cell debris. Protein concentrations were determined by colorimetric assay (Bio-Rad, Hercules, CA, USA). Western blotting assays using 30-50 ug from whole protein lysates are performed using the following primary antibodies: mouse monoclonal αGAPDH (Santa Cruz

Biotech.); rabbit polyclonal αRAD17, αE2F5, αNF-kB (Santa Cruz Biotech.); rabbit polyclonal αH2AX(Phospho-Ser139), αBRCA1 (Cell Signaling Tech., Danvers, MA, USA). The immunodetection was performed with the aid of the enhanced chemiluminescence system (Thermo Fisher Scientific, Rockford, IL, USA). The acquisition of the chemiluminescence has performed by using Alliance 4.7 by UVITEC (Eppendorf). In dot blot assays, 2 ug from whole protein lysates are spotted onto a nitrocellulose membrane (ThermoFisher Scientific) and air-dried. The membrane was blocked in 5% milk/TBST and incubated with the antibodies and the metodologies described above.

RNA isolation, quantitative real-time PCR analysis

Total RNA was extracted from cells using TRI Reagent (Invitrogen, Carlsbad, CA, USA) according to manufacturer's instructions. Five micrograms of total RNA were reverse-transcribed at 37°C for 60 min in the presence of random hexamers and Moloney murine leukemia virus reverse transcriptase (Invitrogen).

To analyze the expression of miR-205-5p, 30 ng RNA was retro-transcribed using TaqMan microRNA Reverse Transcription Kit (Applied Biosystems) and real-time PCR of miR expression was carried out in a final volume of 10ul using TaqMan MicroRNA® Assays (Applied Biosystems) and normalized using *RNU49* and *RNU19* as endogenous controls. TaqMan probes for miRNAs and RNU were purchased from Applied Biosystems.

The RNA expression levels were measured by real-time PCR using the SYBR Green assay (Applied Biosystems, Carlsbad, CA, USA) on a StepOne and Q7 instrument (Applied Biosystems). The sequences of oligonucleotides are listed in Supplementary Table S6. All primer sets worked under identical quantitative PCR cycling conditions with similar efficiencies to obtain simultaneous amplification in the same run. The $2^{-\Delta\Delta CT}$ method for relative quantitation of gene expression was used to determine mRNA expression levels. *GAPDH* and *beta-actin* gene expression were used as endogenous controls to standardize mRNA expression. All reactions were performed in triplicate. P-values were calculated with two-tailed Student's t-test. Statistically significant results were referred with a p-value < 0.05.

Cell viability and colony formation assays

Cell viability was assayed with ATPlite (Perkin Elmer) according to the manufacturer's instructions using the EnSpireMultilabel Reader (Perkin Elmer). Cells (10^4 per well) were plated in triplicate in 96-well plates and treated as indicated.

With regard to colony-forming assays, cells are transfected as indicated in the figure accordingly with the procedures already described. After 24h of transfection, 800 cells from each point were seeded in 12-multiwell plates and grown for 10 days. Cells were stained with crystal violet and colonies evaluated by using ImageJ software (https://imagej.nih.gov/ij/).

Immunofluorescence

Cells were fixed in 4% PBS-paraformaldeyde for 15 min on ice, incubated in 0.5% Triton for 10 min, then in 10% FBS with 0.3% Triton and then stained for 1h with rabbit polyclonal αH2AX(Phospho-Ser139) (Cell Signaling Tech., Danvers, MA, USA) and rabbit polyclonal α53BP1 (Abcam), used at a 1:100 dilution in 2%FBS with 0.1% Triton. Secondary antibody (Alexa Fluor 488, 1:500) was incubated for 40 min. The nuclei were stained with Hoechst for 10 min followed by visualization under a fluorescence microscope.

Boyden chamber migration assay

Cells are transfected as indicated in the figure accordingly with the procedures described above. After 24h of transfection, 50000 cells were suspended in 500 µl serum free medium in transwells (PET membrane of 8 µm pore size, Falcon n. 353097) and placed in 24-well plates containing medium with 10% FBS. After 18 h, chambers were washed and cells were removed from the upper side of the chamber with a cotton swab. Migrated cells were fixed and stained using DAPI cell stain solution (Chemicon International). Images were captured using the 20x objective of the Axiovert 200 microscope (Carl Zeiss) and analyzed using AxioVision software (Carl Zeiss). Representative images are shown. The average number of migrated cells from 10 representative fields (six replicates per condition) was counted under a phase contrast microscope. P-values were calculated with two-tailed Student's t-test. Statistically significant results were referred with a p-value < 0.05.

Flow cytometric analysis of cell cycle

Cells were seeded in triplicate in 6-well plates in a number of 2×10^5 cells per well and transfected as indicated. After 48h of transfection, cells were washed in PBS, fixed in Ethanol solution and stained in a PI solution (50μg PI in 0.1% sodium citrate, 0.1% NP40, pH7.4) for 30 min at 4°C in the dark. Flow cytometry analysis was performed using a Guava® easyCyte flow cytometer (Merck-Millipore). Cell cycle was evaluated by InCyte Guava Cell Cycle Software (Merck-Millipore). Each point were analyzed in at least three different experiments. P-values were calculated with two-tailed Student's t-test. Statistically significant results were referred with a p-value < 0.05.

BrdU incorporation assay

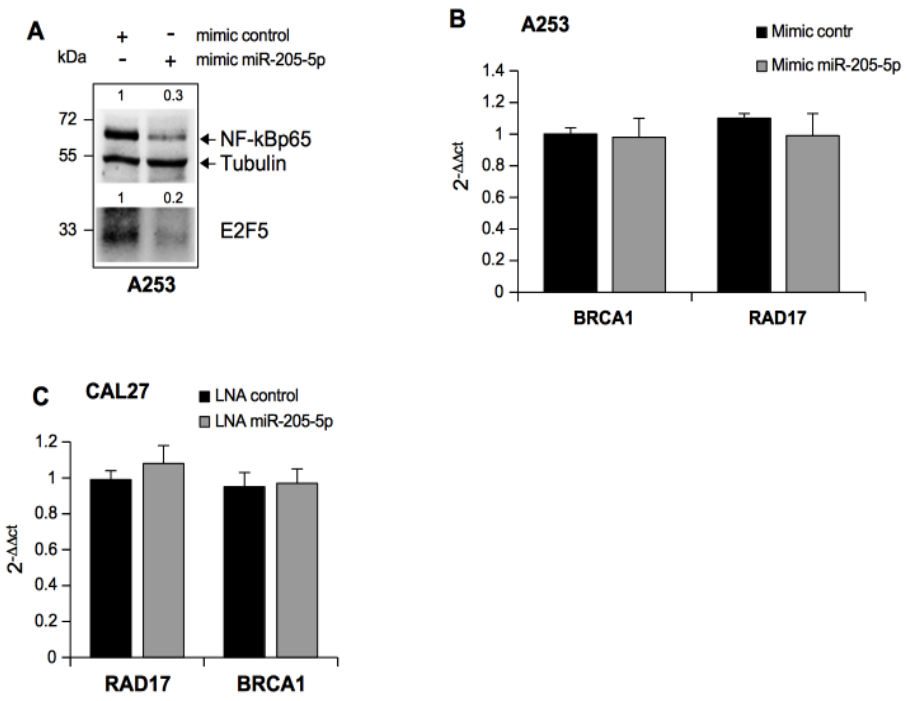
CAL27 cells were seeded onto 22-mm diameter coverglasses placed in 6-well plates (3×10^5 cells/coverglass) and transfected as indicated for 48h. Before to fixing the cells, 10 μM BrdU (Sigma Chemicals) were added to the cultures for 20 minutes. The cells were rinsed and fixed in 4% phosphate-buffered paraformaldehyde for 10 min. Following aspiration, the cells were rinsed 3 times in PBS for 5 min and 0.5% Triton X-100/2N Hcl solution was added to the specimens for 20 min. After neutralization using PBS, the specimens were blocked in mouse serum for 60 min. The blocking solution was aspirated and the specimens were incubated in diluted primary mouse-monoclonal antibody to BrdU (1:25; BD Biosciences n°347580) overnight at 4°C. After rinsing 3 times in PBS for 5 min, the specimens were incubated in fluorochrome-conjugated secondary antibody diluted in PBS at room temperature in the dark and observed under fluorescent microscope. At least 1000 cells/treatment using at least 2 cover-glasses/treatment were counted, and the number of positive cells was recorded. Labeling indexes were calculated as the number of positively stained cells divided by the number of total cells. The total cells for each field was counted using phase contrast light.

Luciferase reporter gene assays

Cells ($2x10^5$) were seeded into 6- or 12-well culture plates and transiently transfected with 100ng of reporter vectors, with mimic miR-205-5p or mimic control or with LNA miR-205-5p or LNA control. 1/10 of CMV-*Renilla* plasmid as an internal control was also co-transfected for transfection efficiency. Cells were harvested 48h post-transfection and luciferase activities were analyzed by the dual-luciferase reporter assay system (Promega, Madison, WI) in the GloMax 96 Microplate Luminometer (Promega). Reporter assays were carried out in quadruplicate and the mean ± S.D. was reported. Statistical significance was analyzed by the unpaired Student *t*-test.

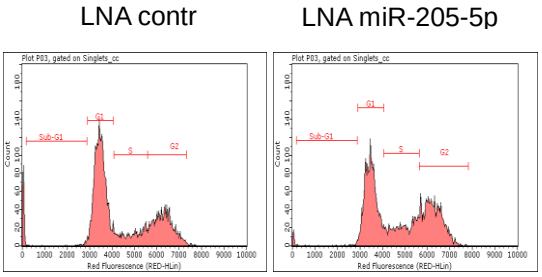
RNA immunoprecipitation (RIP)

Cells were crosslinked with 254 nm UV light 800 mJ/cm2 (using 10 cm dish with 2.5 ml PBS). Nuclei were isolated and resuspended in lysis buffer (Tris-HCl pH 7.5 50 mM, EDTA 1 mM, SDS 0.5%, DTT 1 mM), using 200 µl for each planned IP sample, and sonicated to obtain a smear not higher than 500 bp. Lysate was treated with DNase (DNAfree, Ambion) and diluted with 400 µl of correction buffer (NP-40, 0.625%, DOC, 0.312%, MgCl2, 5.6 mM, Tris-HCl pH 7.5, 47.5 mM, NaCl, 187.5 mM, glycerol, 12.5%, DTT 1 mM). IP was carried out overnight at +4°C. The following ChIP-grade antibodies were employed: 10686-1-AP Proteintech (AGO2); IgG as control. IP washing and proteinase K digestion were carried out as ChIP protocol (18), crosslinking was reversed by incubation at 70°C for 30 min, and RNA was recovered by TRIzol extraction.



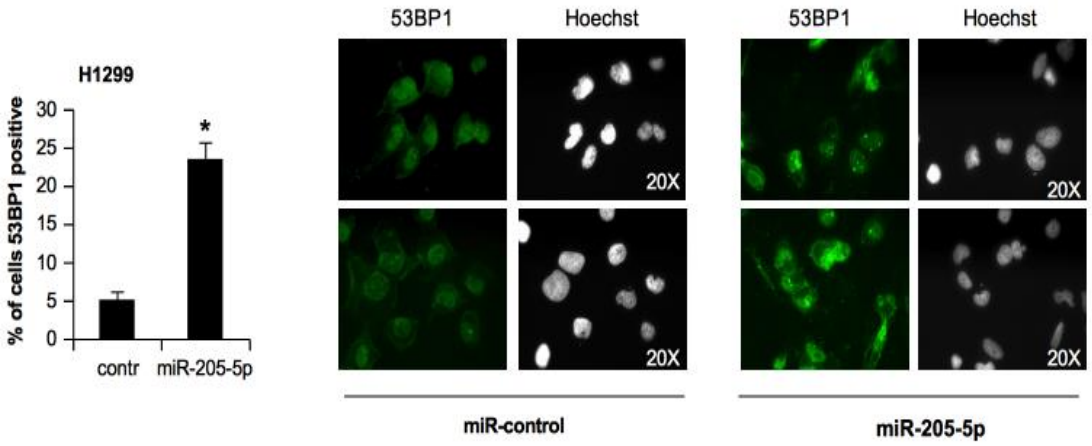
Supplementary Figure 1

Supplementary Figure 1: (A) Representive immunoblotting analysis of NF-kBp65, E2F5 and Tubulin (loading control) protein expression in A253 cells transfected with mimic miR-205-5p and mimic control oligos. (B) *Rad17* and *Brca1* mRNA expression was analyzed by RT-qPCR in A253 cells transfected with either mimic control and mimic miR-205-5p oligos. Bars represent mean ± s.d. from three biological replicates. P-values were calculated with two-tailed t-test and they were higher than the significance level of 0.05. (C) *Rad17* and *Brca1* mRNA expression was analyzed by RT-qPCR in CAL27 cells transfected with either LNA control and LNA miR-205-5p oligos. Bars represent mean ± s.d. from three biological replicates. P-values were calculated with two-tailed t-test and they were higher than the significance level of 0.05.



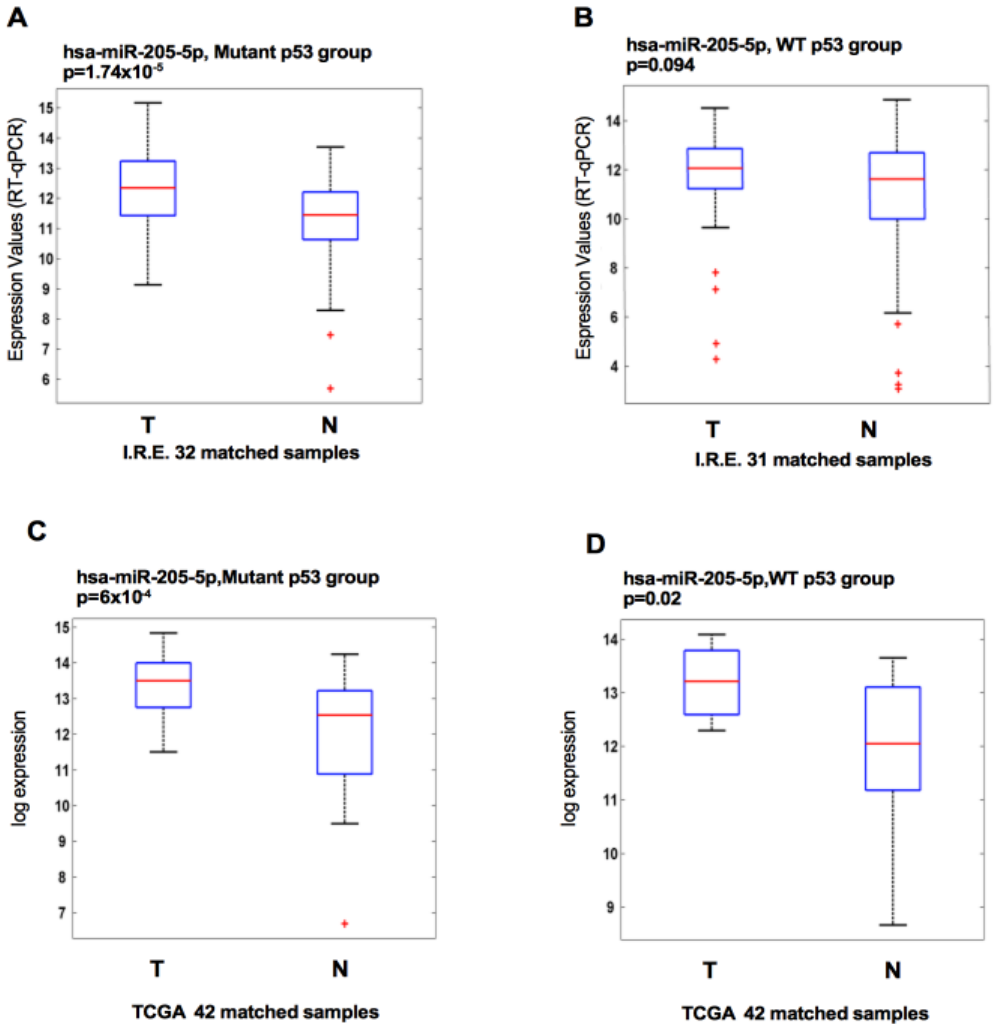
CAL27

Supplementary Figure 2: Representative cell population histogram of CAL27 transfected with LNA control and LNA miR-205-5p oligos and analysed in the figure 2B.



Supplementary Figure 3

Supplementary Figure 3: (A) H1299 cells are transfected with mimic miR-205-5p and mimic control oligos. Cells are then analyzed by 53BP1 staining 48 h after overexpression. Representative images and quantification of cells with 53BP1 foci are shown. Hoechst was used for nuclear staining. P-values were calculated with two-tailed t-test. Statistically significant results were with *p-value < 0.02 Data represent the mean±s.d. from three biological replicates.



Supplementary Figure 4

Supplementary Figure 4: (A and B) RT-qPCR in cDNA obtained from each non-tumoral (N) and matched tumoral (T) tissues and analyzed in the sub-group of HNSCC patients (Regina Elena National Cancer Institute cohort) carrying missense mutations in the *TP53* gene (A) and in the sub-group of HNSCC patients with wild type *TP53* gene (B). (B and C) Box-plot analysis performed in HNSCC from TCGA. It is represented the association of miR-205-5p expression levels with the tumoral and no n-tumoral matched tissues analyzed in the sub-group of HNSCC patients carrying missense mutations in the *TP53* gene (B) and in the sub-group of HNSCC patients with wild type *TP53* gene (C).

Supplementary Table S1

Comparative view of predicted miRNA sites on 3' UTR region by miRWalk & other prediction programs

Note : The below table displays all putative miRNA sites produced by both miRWalk and other programs i.e. contains all the putative targets of other programs.

Gene Name	MicroRNA	StemLoop ID	DIANAmT	miRanda	miRDB	miRWalk	RNAhybrid	PICTAR4	RNA22	Targetscan	SUM
RAD17	hsa-miR-205	hsa-mir-205	1	1	0	1	1	0	0	1	5
RAD17	hsa-miR-129-5p	hsa-mir-129-1	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-124	hsa-mir-124-2	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-362-3p	hsa-mir-362	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-452	hsa-mir-452	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-495	hsa-mir-495	1	0	1	1	0	0	0	1	4
RAD17	hsa-miR-653	hsa-mir-653	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-578	hsa-mir-578	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-205	hsa-mir-205	1	0	0	1	1	0	0	1	4
RAD17	hsa-miR-603	hsa-mir-603	1	1	0	1	0	0	0	1	4
RAD17	hsa-miR-124	hsa-mir-124-3	1	1	0	1	0	0	0	1	4

Comparative view of predicted miRNA sites on 3' UTR region by miRWalk & other prediction programs

Note : The below table displays all putative miRNA sites produced by both miRWalk and other programs i.e. contains all the putative targets of other programs.

Gene Name	MicroRNA	StemLoop ID	DIANAmT	miRanda	miRDB	miRWalk	RNAhybrid	PICTAR4	RNA22	Targetscan	SUM
BRCA1	hsa-miR-205	hsa-mir-205	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-125a-3p	hsa-mir-125a	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-106b	hsa-mir-106b	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-28-5p	hsa-mir-28	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-197	hsa-mir-197	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-220c	hsa-mir-220c	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-519d	hsa-mir-519d	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-516a-3p	hsa-mir-516a-1	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-302b	hsa-mir-302b	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-590-3p	hsa-mir-590	1	1	0	1	0	0	0	1	4
BRCA1	hsa-miR-629	hsa-mir-629	1	1	0	1	0	0	0	1	4

Supplementary Table S2

	Folds T/N		Tumors	
	R	p-val	R	p-val
BRCA1/RAD17	0,7149	9,65E-011	0,7105	1,41E-010

Results of Pearson correlation analysis relative to BRCA1 and RAD17 in 522 HNSCC samples from TCGA (478T).

Supplementary Table S3

BRCA1/RAD17 signature				
	high\high	low\low	high\low	low\high
mutp53	1	19	0	6
wtp53	10	4	7	10
tot	11	23	7	16

chi2 pval(4 groups)=1E-05
fisher exact test(high\high vs low\low)=7E-05

Results of Fisher analysis relative to the dipendence of BRCA1 and RAD17 expression in the HNSCC mutp53 and wtp53 subgroups from TCGA used in in the recurrence analysis of Fig. 6g (57T). High: z-score > 0; low: z-score < 0.

Supplementary Table S4

miR-205-5p\RAD17		
	high\low	others
mutp53	11	15
wtp53	5	26

fisher exact test=0.039

miR-205-5p\BRCA1		
	high\low	others
mutp53	9	17
wtp53	2	29

fisher exact test=0.016

Results of Fisher analysis relative to the dipendence of miR-205\BRCA1 and miR-205\RAD17 expression in the HNSCC mutp53 and wtp53 subgroups from TCGA used in in the recurrence analysis of Fig. 6g (57T). High: z-score > 0; low: z-score < 0.

Supplementary Table S5

Primers used to clone RAD17 3'UTR in psiCHEK2 vector

RAD17 XhoI FW	5'- AACTCGAGAATAATAGAAGACTACGAGA -3'
RAD17 NotI RV	5'- AAGCGGCCGCTTTTGGAAAGAGTTTACAGT -3'

Primers used for miR-205-5p seed sequence RAD17 3'UTR deletion in psiCHEK2 vector

Primer Name	Primer Sequence (5' to 3')
del124-126-antisense	5'-tttttgcatcctgaattagtcctcatcttgatatttggcataatgt-3'
del124-126	5'-acattatgccaaatatcaagatgaggactaattcaggatgcaaaaa-3'

Primer-template duplexes:

Primer Name	Primer-Template Duplex
del124-126-antisense	tgaacattatgccaaatatcaagatgtgaaggactaattcaggatgcaaaaacgt |||||||||||||||||||| |||||||||||||||||||| 3'-tgtaatacggtttatagttctac---tcctgattaagtcctacgttttt-5'
del124-126	5'-acattatgccaaatatcaagatg---aggactaattcaggatgcaaaaa-3' |||||||||||||||||||| |||||||||||||||||||| acttgtaatacggtttatagttctacacttcctgattaagtcctacgttttgca

Primers used for miR-205-5p seed sequence BRCA1 3'UTR deletion in psiCHEK2 vector

Primer Name	Primer Sequence (5' to 3')
del231-233	5'-gaaaaggacttctggctcaagggtcccttaaaga-3'
del231-233-antisense	5'-tctttaagggacccttgagccagaagtccttttc-3'

Primer-template duplexes:

Primer Name	Primer-Template Duplex
del231-233	5'-gaaaaggacttctggct---caagggtcccttaaaga-3' |||||||||||||||| |||||||||||||||| ggacttttcctgaagaccgatacgttcccagggaatttctaaa
del231-233-antisense	cctgaaaaggacttctggctatgcaagggtcccttaaagattt |||||||||||||||| |||||||||||||||| 3'-cttttcctgaagaccga---gttcccagggaatttct-5'

Supplementary Table S6

Primer sequences for amplification of cDNAs in Real Time qPCR experiments

GAPDH FW [PMID: 23125021]	5'- GAGTCAACGGATTTGGTCGT -3'
GAPDH RV RV [PMID: 23125021]	5'- GAGTCAACGGATTTGGTCGT -3'
Actin FW [doi: 10.7150/thno.22167]	5'- GAGGCCCAGAGCAAGAGAG -3'
Actin RV [doi: 10.7150/thno.22167]	5'- AGGTGTGGTGCCAGATTTTC -3'
Pre-miR-205-5p FW [doi: 10.7150/thno.22167]	5'- TCATTCCACCGGAGTCTGT -3'
Pre-miR-205-5p RV [doi: 10.7150/thno.22167	5'- AGCTCCATGCCTCCTGAACT -3'
BRCA1 FW [PMID: 25650659]	5′- TCCCATCTGTCTGGAGTTGA -3′
BRCA1 RV [PMID: 25650659]	5′- TGTGAAGGCCCTTTCTTCTG -3′
RAD17 FW [PMID: 25650659]	5′- GGAGCATGGTATTCAAGTACAAG -3′
RAD17 RV [PMID: 25650659]	5′- GGGAAACATATGGAAGCTTGA -3′

Supplementary Table S7

patient number	codon	Type of mutation
'5'	H193Y	missense
'18'	V157I, R158H	missense
'69'	N247 in frame	framshift
'84'	F106 in frame	framshift
'105'	H179R	missense
'93'	del. 4 bp introne 8	frameshift
'3'	wt	
'87'	wt	
'90'	wt	
'15'	wt	
'45'	del. 3bp exon 9	frameshift
'12'	wt	
'115'	wt	
'109'	C275R	missense
'97'	wt	
'120'	wt	
'71'	wt	
'101'	R213X	nonsense
'86'	I255F	missense
'104'	H179R	missense
'99'	E198X	nonsense
'28'	P278T	missense
'29'	R156H; C275S; R282Q	missense
'49'	E198X	nonsense
'17'	R196X	nonsense
'61'	V157T	missense
'82'	del 2 bp P152-E153 not in frame	frameshift
'70'	S183X	nonsense
'74'	slice site exon 9	splice site
'42'	wt	
'8'	wt	
'7'	G266R	missense
'66'	del 1bp exon 4 not inframe	frameshift
'113'	R196X	nonsense
'63'	P273C	missense
'88'	del 4 bp exon 8	framshift
'54'	wt	
'48'	wt	
'14'	P278S	missense
'37'	W146X	nonsense
'22'	R248Q	missense
'59'	H193R	missense
'58'	ins 1 bp not in frame	frameshift
'51'	Y234C	missense
'55'	Y205C	missense
'36'	wt	
'107'	wt	
'57'	wt	
'102'	wt	
'10'	wt	
'1'	wt	
'2'	wt	
'40'	wt	
'44'	wt	
'41'	wt	
'112'	wt	
'73'	wt	
'32'	wt	
'65'	wt	
'60'	wt	
'114'	wt	
'67'	wt	
'33'	wt	

Mutational status of TP53 gene of HNSCC tumors (cohort of Regina Elena National cancer Institute)

Figure 1C

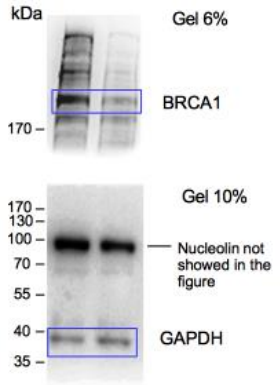


Figure 3B

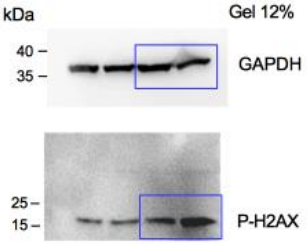


Figure 3D

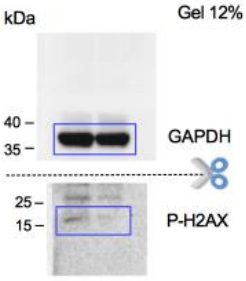


Figure 3H

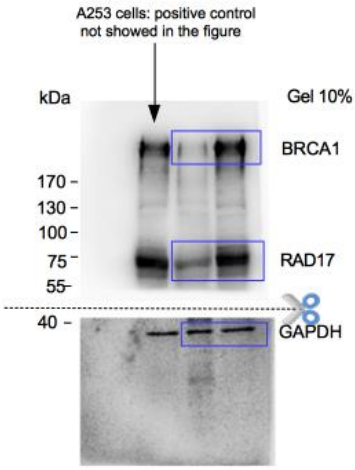
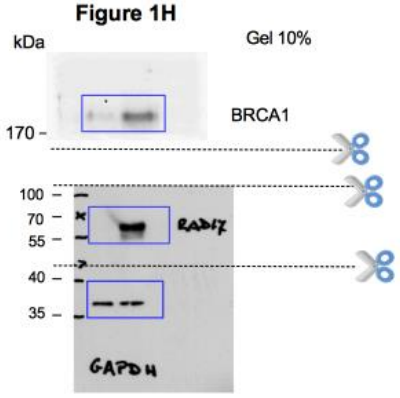
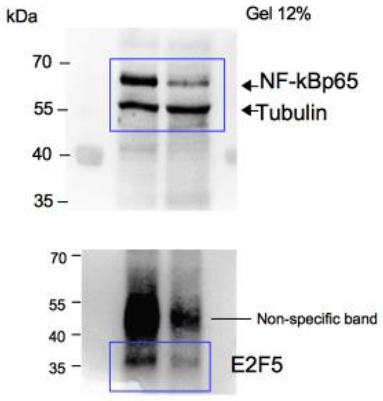


Figure 1H



Supplementary Figure S1A



Acquisition by Uvitec-Eppendorf

Blank informed consent

MODULO DI CONSENSO INFORMATO

STUDIO DEL PROFILO DI ESPRESSIONE DI microRNA IN CARCINOMI SQUAMOSI DELLA TESTA E DEL COLLO E NEI TESSUTI AUTOLOGHI PERI-TUMORALE E LONTANO

Nota informativa

1. **Presentazione e obiettivi della sperimentazione**

In questo Istituto si sta svolgendo una sperimentazione clinica dal titolo: **STUDIO DEL PROFILO DI ESPRESSIONE DEI microRNA IN CARCINOMI SQUAMOSI DELLA TESTA E DEL COLLO E NEI TESSUTI AUTOLOGHI PERI-TUMORALE E LONTANO**

L'obiettivo generale di tale sperimentazione è individuare gruppi di microRNA con valore diagnostico, prognostico o predittivo per i tumori testa/collo. Per raggiungere questo traguardo, si chiede la Sua partecipazione, al fine di costituire un idoneo archivio di frammenti di tessuti da utilizzare per il progresso delle conoscenze in campo medico. La Sua partecipazione alla sperimentazione contribuirà allo sviluppo di nuove possibilità diagnostiche e/o terapeutiche per i pazienti affetti da tumore testa/collo.

L'esecuzione di questo studio è stata **approvata dal Comitato Etico degli I.F.O**. e **sarà condotta conformemente alle Norme di Buona Pratica Clinica**, al fine di assicurare la salvaguardia dei diritti, dell'integrità e del benessere dei soggetti coinvolti nella sperimentazione.

2. **Procedure sperimentali**

Nell'ambito delle procedure di terapia chirurgica che le sono state prescritte dai Suoi Medici Curanti, **e senza che questo comporti alcuna modifica nelle procedure che sono necessarie per il trattamento della sua patologia,** un piccolo frammento di tessuto, **che non potrebbe essere altrimenti impiegato**, sarà utilizzato per analisi di laboratorio e studi di biologia molecolare. Nel contesto delle normali visite di controllo che i Suoi Medici curanti riterranno opportune nel Suo caso, potrebbe inoltre essere effettuato un prelievo di sangue aggiuntivo, sempre per gli stessi motivi.

3. **Rischi e benefici**

Mentre **resta categoricamente escluso qualsiasi rischio** per Lei (il prelievo di un piccolo frammento di tessuto non comporta alcuna modifica nelle procedure chirurgiche), non sono attesi nemmeno benefici, quantomeno immediati o diretti. Consideri, comunque, che qualsiasi informazione e risultato ottenuto dallo studio saranno in futuro utili anche a pazienti affetti dalla Sua stessa malattia.

4. **Riservatezza dei dati clinici**

Qualora volesse partecipare alla sperimentazione, i Suoi dati personali saranno sempre trattati in modo strettamente confidenziale e non saranno resi pubblici. Il proponente la sperimentazione (ovvero l'Unità di Oncogenomica Translazionale, che lavora presso il nostro Ente, e che è composto da ricercatori clinici e sperimentali) potrà infatti esaminare i Suoi dati clinici, al fine di divulgare i risultati dello studio secondo i consueti metodi scientifici, ma il Suo nome non potrà essere identificato, come richiesto dalla legge italiana sulla Privacy (D. Lgs 196/2003).

5. **Aspetti finanziari**

La partecipazione alla sperimentazione non comporta alcun onere finanziario e non prevede alcun compenso.

La copertura **assicurativa** per i danni eventualmente derivanti dalla sperimentazione è assicurata dagli I.F.O.

6. **Partecipazione alla sperimentazione**

La Sua partecipazione a questo studio è del tutto **volontaria**. Lei potrà rifiutarsi di donare frammenti di tessuto, senza che ciò comporti alcuna riduzione della normale attenzione terapeutica ed assistenziale dovuta.

7. **Altre informazioni**

In caso di partecipazione alla sperimentazione, Lei potrà chiedere in qualsiasi momento informazioni ulteriori sullo studio clinico e sui progressi conseguiti, così come sarà tempestivamente informato qualora divengano disponibili informazioni che possano influenzare la Sua volontà a continuare la partecipazione allo studio.

Per qualsiasi informazione Lei potrà rivolgersi ai seguenti medici:

Dott. …… tel. ……..

Dott. …… tel. ……..

L'esecuzione di questo studio è stata approvata dal Comitato Etico I.F.O. e sarà condotta conformemente alle norme di Buona Pratica Clinica. Lei potrà accedere alla documentazione assicurativa relativa alla sperimentazione in oggetto, al parere espresso dal Comitato Etico degli I.F.O. e potrà avere dal medico sperimentatore qualsiasi informazione inerente alla sperimentazione in oggetto. Se vuole può contattare direttamente il Comitato Etico per segnalare ogni eventuale difformità tra lo studio cui Lei partecipa e le informazioni ricevute prima di prestare il Suo consenso (il Comitato Etico ha sede in Via Elio Chianesi, 53 Roma tel. 06-5266.2719).

DICHIARAZIONE DEL CONSENSO

STUDIO DEL PROFILO DI ESPRESSIONE DI microRNA IN CARCINOMI SQUAMOSI DELLA TESTA E DEL COLLO E NEI TESSUTI AUTOLOGHI PERI-TUMORALE E LONTANO

Io sottoscritto _____

dichiaro di aver ricevuto dal Dr. _____

esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca dal titolo "**STUDIO DEL PROFILO DI ESPRESSIONE DI microRNA IN CARCINOMI SQUAMOSI DELLA TESTA E DEL COLLO E NEI TESSUTI AUTOLOGHI PERI-TUMORALE E LONTANO**", secondo quanto riportato nella scheda informativa qui allegata, copia della quale mi è stata consegnata **almeno 24 ore prima** della firma del presente consenso (formato da un numero totale di 3 pagine).

Dichiaro altresì di aver potuto discutere tali spiegazioni, porre tutte le domande che ho ritenuto necessarie e di aver ricevuto risposte soddisfacenti, come pure di aver avuto il tempo per informarmi in merito ai particolari dello studio con persona di mia fiducia.

Sono stato informato/a, inoltre, del mio diritto ad avere libero accesso alla documentazione relativa alla ricerca ed alla valutazione espressa dal Comitato Etico.

Accetto dunque liberamente di partecipare alla ricerca, avendo compreso completamente il significato della richiesta ed i rischi e benefici che possono derivare da tale partecipazione.

Acconsento/NON acconsento (cancellare una delle due opzioni, come desiderato) che lo Sperimentatore o il Medico sopra menzionato informi il mio Medico di famiglia circa la mia partecipazione a questo studio clinico

_____ _____

Data/ora Firma del medico che ha informato il paziente

Data/ora Firma per consenso del paziente/rappresentante legale

(Nel caso in cui il paziente non possa firmare)

Io sottoscritto _____

testimonio che il Dr. _____

ha esaurientemente spiegato al Sig. _____

le caratteristiche dello studio in oggetto, secondo quanto riportato nella scheda informativa qui allegata, e che lo stesso, avendo avuto la possibilità di fare tutte le domande che ha ritenuto necessarie, ha accettato liberamente di partecipare.

Data/ora Firma del testimone indipendente