miRNA	Regulation	Fold increase / decrease	P value
hsa-miR-146b-5p	up	3,82	0,0094
hsa-miR-1977	up	2,34	0,0345
hsa-miR-181a*	up	2,20	0,0174
hsa-miR-193b*	up	2,14	0,0243
hsa-miR-141	up	1,98	0,0046
hsa-miR-1973	up	1,92	0,0229
hsa-miR-29b-1*	up	1,77	0,0033
hsa-miR-125b	up	1,72	0,0322
hsa-miR-21*	up	1,71	0,0213
hsa-miR-491-3p	up	1,69	0,0001
hsa-miR-30c	up	1,68	0,0203
hsa-miR-200a*	up	1,64	0,0189
hsa-miR-30e	up	1,54	0,0450
hsa-miR-200c*	up	1,53	0,0424
hsa-miR-1275	up	1,53	0,0002
hsa-miR-183*	down	3,34	0,0037
hsa-miR-501-3p	down	2,65	0,0046
hsa-miR-345	down	2,63	0,0140
hsa-miR-18a	down	2,27	0,0071
hsa-miR-194	down	2,07	0,0429
hsa-miR-33a	down	2,06	0,0005
hsa-miR-218	down	1,99	0,0341
hsa-miR-32	down	1,94	0,0046
hsa-miR-17	down	1,93	0,0205
hsa-miR-18b	down	1,84	0,0169
hsa-miR-19a	down	1,83	0,0115
hsa-miR-19b	down	1,83	0,0109
hsa-miR-7	down	1,82	0,0388
hsa-miR-192	down	1,77	0,0072
hsa-miR-19b-1*	down	1,75	0,0011
hsa-miR-101	down	1,70	0,0301
hsa-miR-362-3p	down	1,70	0,0051
hsa-miR-769-5p	down	1,64	0,0164
hsa-miR-20a	down	1,62	0,0339
hsa-miR-15b	down	1,61	0,0207
hsa-miR-590-5p	down	1,57	0,0243
hsa-miR-503	down	1,54	0,0283
hsa-miR-219-5p	down	1,52	0,0284

Suppl. Table 1: miRNAs differentially regulated upon TACC3 depletion in MCF7 cells thereby undergoing premature senescence.

Analysis of differentially expressed miRNAs using the Genespring software (ver11) (expression changes \geq 1.5-fold were determined four days after DOX-induced TACC3 shRNA expression that triggers premature senescence; p<0.05; student's t-test).

Suppl. Table 2: Overview of the number of differentially regulated, putative miRNA target genes *vs.* the total number of candidate miRNA target genes.

	miRNA	Differentially regulated putative target genes	Candidate target genes (total)	P value	
1	hsa-miR-17	138	1601	0,000011	
2	hsa-miR-20a	138	1594	0,000008	
3	hsa-miR-30e	129	1445	0,000004	
4	hsa-miR-30c	124	1440	0,000031	
5	hsa-miR-19a	124	1385	0,000004	
6	hsa-miR-19b	124	1383	0,000004	
7	hsa-miR-15b	108	1359	0,001533	
8	hsa-miR-21*	99	1345	0,021258	
9	hsa-miR-32	96	992	0,000002	
10	hsa-miR-218	75	928	0,005707	
11	hsa-miR-101	65	855	0,032452	
12	hsa-miR-125b	61	845	0,088203	
13	hsa-miR-7	53	473	0,000007	
14	hsa-miR-503	35	355	0,002857	
15	hsa-miR-18a	32	320	0,003698	
16	hsa-miR-18b	32	32 320		
17	hsa-miR-590-5p	30	307	0,006633	
18	hsa-miR-219-5p	29	417	0,342896	
19	hsa-miR-491-3p	25	278	0,028984	
20	hsa-miR-194	23 363		0,651865	
21	hsa-miR-362-3p	21	327	0,634296	
22	hsa-miR-146b- 5p	20	168	0,002443	
23	hsa-miR-33a	15 376		0,148934	
24	hsa-miR-192	13	125	0,051686	
25	hsa-miR-345	11	140	0,277760	
26	hsa-miR-501-3p	9	241	0,211704	
27	hsa-miR-769-5p	7	126	1,000000	
28	hsa-miR-1275	3	90	0,493812	

Analysis of putative target mRNAs differentially regulated by miRNAs was performed using the Genespring software (ver11). Expression changes \geq 1.75 were determined four days after DOX-induced TACC3 shRNA expression and senescence induction (p \leq 0.05; student's t-test). As indicated in the last column, significant correlations between the total number of putative target mRNAs *vs*. the number of differentially expressed candidate target mRNAs were determined using Fisher's exact test (p \leq 0.05) and a Bonferroni correction (highly significant miRNA-mRNA correlations with p \leq 0.0018 are indicated in bold).

TACC3 depletion (TACC3 shRNA *vs.* control shRNA, day 4 of DOX treatment)



Β

Α

γIR (20 Gy) vs. control (day 4)



Merge (MTCO2 / SIRT4)



sham







Gene Human SIRT4 NM_012240 3' UTR length:205 Conserved sites for miRNA families broadly conserved among vertebrates <u>miR-1</u>5/16/195/424/497 Conserved sites for miRNA families conserved only among mammals Poorly conserved sites and sites for poorly conserved miRNA families miR-1299 miR-1274b miR-503 miR-1300 miR-582-3p/1267 miR-1284 miR-320/320abc miR-344-5p/484 miR-1274a miR-646 miR-579 miR-653 miR-148/152 miR-875-3p.h miR-26ab/1297 miR-1253 miR-1292 miR-223 miR-516b miR-339-5p miR-580 miR-616 ..20.. ...30...40..... .70. .80..90. .100. .10... Hsa CCACAGCCUG-AUAUUCCAGAACCUGGAACAGGGACUUUCACUUGAAUCUGCUGCUAAAUGUAAA-----U----GCCUUCUCAAAUGACAGAUUCC--AGUUCCCAUUCAACAG----AGU Ptr CCACAGCCUG-AUAUUCCAGAACCUGGAACAGGGACUUUCACUUGAAUCUUGCUGCUAAAUGUAAA-----U----GCCUUCUCAAAUGACAGAUUCC--AGUUCCCAUUCAACAG---AGU Mml 0ga Tbe Mmu CAGCACUCUG-AUGUCCAAAGGCUGGAAA--UGAACUUUCCUCUGAGUUCCGCUGCUCAAGGUAAAGAGAAA-----GCCCUCUCAGGUAAAGGGGUCUAG---Rno CAGCACCCUG-AUGUCCAAAGGCUGGAAA---GGACUUUCCUUUGGGUCCCGCUGCUAAAGGUAAAGAG--A----GCCCUUUCAGA---UUCCUGGU-ACACCUAGUAGU CUGCCCAUCCUAGGCCAGAACA--GGGACCUUACUUCCAAUCCUGCUGUUGAAGGUAAA--U----GCCCUUUUA Сро CCACAGO ---CAGCCUG-AUGUUCCUGAUCCAGAAACUGGGUCUUUCAACUUGAAUCUGCUGCCAAAGGUAGG----U----GCCUUCUCAGGUCCUAG-----UACCACGUGACUAAGAGUAGG 0cu Sar Eeu Cfa CCACAACCUG-AUGUUUCUGAGCCAGAAACUGGGACUUUCACUUUAAUC---CUAUUAAAGGUAAG----UUAAAGGCUUUCUUAGAUACCAGUUUCCAG--UUUGCAUUCAA Fca Eca CCACAGCCUG-AUGUUCCUGCGCCGGAAACUGGAAUUUCCACUUGAAUCCUGCUGCUAAAGGUAAA-----U----GCCUUCUCAGAUAUCAGAUGCCAG--UUUCCAGUCAA--Bta Dno CUACAGAGAGAC-AUGUUCCCAAGCCAGAAACAGGGAUUUUCACUGGAAUUCUGCUGCUAAAGAUAAA-----U----GCCUUCACAGACAUCAGAUUCCAG--CUCCCACUCAACAG---AGGGC Laf Ete Mdo 0an CCGGAGCCUC-ACGGGCCCCGCUCGGACA--GGGA--Aca CC-CAGCUCG-GCACCC-----Gga Xtr miR-15/16/195/424/497

http://www.targetscan.org/cgi-bin/vert_50/view_gene.cgi?gs=SIRT4&taxid=9606&members=&showcnc=1&shownc=1

R

Human SIRT4 3' UTR miRNA Table Table sorted by total context score

[Sort table by aggregate P_{CT}]

miRNA families broadly conserved among vertebrates

	conserved sites		poorly conserved sites			Total	Aggregate			
miRNA	Total	8mer	7mer-m8	7mer-1A	Total	8mer	7mer-m8	7mer-1A	Context score	P _{CT}
miR-15/16/195/424/497	1	1	0	0	0	0	0	0	-0.47	< 0.1
miR-148/152	0	0	0	0	1	1	0	0	-0.32	0.22
miR-503	0	0	0	0	1	0	0	1	-0.20	< 0.1
miR-26ab/1297	0	0	0	0	1	0	0	1	-0.16	< 0.1
miR-223	0	0	0	0	1	0	0	1	-0.13	0.20

http://www.targetscan.org/cgi-bin/vert_50/view_genetable.cgi?gs=SIRT4&taxid=9606&members=&showcnc=1&shownc=1&sortText=cs









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