Landes Bioscience www.landesbioscience.com

Supplemental Material to:

Minlee Kim, Xiaowei Chen, Lena J Chin, Trupti Paranjape, William C Speed, Kenneth K Kidd, Hongyu Zhao, Joanne B Weidhaas, Frank J Slack

Extensive sequence variation in the 3′ untranslated region of the KRAS gene in lung and ovarian cancer cases

Cell Cycle 2014; 13(6)
http://dx.doi.org/10.4161/cc.27941

http://www.landesbioscience.com/journals/cc/article/27941

SNP ID	chr12 (hg19)	Ancestral allele	Derived allele	Putative miRNA binding sites	Disease	Association with the derived allele	Reference
rs12245 (previously rs10771184)	25358650	A	T	miR-544	Ovarian cancer	Increased cancer risk, increased survival, favorable treatment outcome	Liang et al., 2010
rs13096	25359841	T	C	Not specified in the study	Endometriosis	Not associated with risk	Zhao et al., 2006
rs61764370	25360224	A	C	*let-7* (LCS6)	NSCLC	Increased risk	Chin et al., 2008
rs61764370	25360224	A	C	*let-7* (LCS6)	NSCLC	No association with risk and survival	Nelson et al., 2010
rs61764370	25360224	A	C	*let-7* (LCS6)	EOC	Increased risk	Ratner et al., 2010
rs61764370	25360224	A	C	*let-7* (LCS6)	EOC	Not associated with risk	Pharoah et al., 2011
rs61764370	25360224	A	C	*let-7* (LCS6)	Triple-negative breast cancer	Increased risk	Paranjape et al., 2011
rs61764370	25360224	A	C	*let-7* (LCS6)	Breast cancer	Not associated with risk	Hollestelle et al, 2011
rs61764370	25360224	A	C	*let-7* (LCS6)	Breast cancer	HER2-overexpressed cases with hormone replacement therapy	Cerne et al., 2012
rs61764370	25360224	A	C	*let-7* (LCS6)	Oral cancer	Reduced survival	Christensen et al., 2009
rs61764370	25360224	A	C	*let-7* (LCS6)	Colorectal cancer	Better survival in early stages	Smits et al., 2011
rs61764370	25360224	A	C	*let-7* (LCS6)	Colorectal cancer	Reduced survival in late stages	Ryan et al., 2012
rs61764370	25360224	A	C	*let-7* (LCS6)	Colorectal cancer	Favorable cetuximab monotherapy in metastatic cases, increased survival	Zhang et al., 2011
rs61764370	25360224	A	C	*let-7* (LCS6)	Colorectal cancer	Reduced survival in metastatic cases treated with cetuximab-irinotecan	Graziano et al, 2010
rs61764370	25360224	A	C	*let-7* (LCS6)	Colorectal cancer	Unfavorable response to anti-EGFR therapies in metastatic cases	Sebio et al., 2013
rs61764370	25360224	A	C	*let-7* (LCS6)	Endometriosis	Increased risk	Grechukhina et al., 2012
rs61764370	25360225	A	C	*let-7* (LCS6)	Endometriosis	Not associated with risk	Luong et al., 2012
rs9266	25362217	A	G	Not specified in the study	Endometriosis	Not associated with risk	Zhao et al., 2006
rs712	25362552	A	C	*let-7* (LCS1)	Oral squamous cell carcinoma	Decreased risk (with G/T and T/T)	Wang et al., 2011
rs712	25362552	A	C	*let-7* (LCS1)	Gastric cancer	Increased risk with T/T	Li et al., 2013
rs712	25362552	A	C	*let-7* (LCS1)	Colorectal cancer	Increased risk with T/T	Pan et al., 2013

Sup. Table 1. The reported diseases-associated SNPs in the 3' UTR of *KRAS*. Five SNPs have been reported to be associated with diseases to date. NSCLC: non-small cell lung cancer. EOC: epithelial ovarian cancer. LCS: *let-7* complementary site.

	chr12 (hg19)	SNP ID	Putative miRNA complementary sites	LCS	Ago binding
1	25362552	rs712	miR-422a, miR-330-5p, miR-3125, miR-877, miR-378bc, miR-1299, miR-193b, miR-200bc, miR-429	✓ (LCS1)	✓
2	25362536	rs150334904	miR-330-5p, miR-326, miR-4314, miR-1299		✓
3	25362465	rs4285970	501-3p, miR-502-3p,miR-217, miR-4323		
4	25362422	rs1141947	miR-181abcd, miR-23ab, miR-377, miR-543, miR-4262		✓
5	25362325	rs140080026	miR-493		✓
6	25362229	rs61763588	miR-181abcd, miR-425, miR-549		✓
7	25362217	rs9266	miR-181abcd, miR-4262, miR-132		✓
8	25362018	rs188697761	miR-346, miR-873		
9	25361978	rs184195260	miR-4323, miR-2054		✓
10	25361905	rs61763589	miR-384, miR-202*, miR-590-3p, miR-580		
11	25361756	rs61763590	miR-133ab, miR-421		
12	25361667	rs61763591	miR-200a, miR-141, miR-425, miR-3166		
13	25361646	rs7960917			
14	25361589	rs61764365	miR-219-5p	✓ (LCS9)	
15	25361472	rs190606609	miR-96, miR-182, miR-1271, miR-96, miR-431		
16	25361412	rs186283516	miR-146a, miR-146b-5p, miR-219-5p		
17	25361189	rs61764366			
18	25361142	rs7973450	miR-143, miR-302c*		✓
19	25361091	rs4597149	miR-410, miR-340, miR-376c		✓
20	25361074	rs7973623	miR-501-5p		✓
21	25360979	rs113446944	miR-412, miR-340, miR-410		
22	25360964	rs115968671	miR-340, miR-410, miR-3167, miR-607		
23	25360580	rs1141948	miR-145*		
24	25360559	rs61764367	miR-145*		
25	25360545	rs61764368	miR-630, miR-665,		
26	25360358	rs61764369		✓ (LCS4)	
27	25360342	rs140231179	miR-486-5p		
28	25360224	rs61764370	miR-18ab	✓ (LCS6)	
29	25360138	rs4963858	miR-599, miR-148ab, miR-152, miR-199ab-5p		
30	25360098	rs190084851			

31	25360091	rs76218271			
32	25360082	rs149693994			
33	25360078	rs1141949			
34	25359927	rs186623679	miR-142-5p, miR-573, miR-526b*, miR-548k, miR-562, miR-20a, miR-93, miR-302c, miR-373, miR-520b, miR-520c-3p, miR-1		
35	25359919	rs180766260	miR-142-5p, miR-573, miR-526b*, miR-548k, miR-20a, miR-93		
36	25359898	rs191137453	miR-26a,b		
37	25359841	rs13096	miR-101, miR-144, miR-493*, let-7a-2*, let-7g*		✓
38	25359688	rs187126935			
39	25359577	rs61764371	let-7 family, miR-202	✓ (LCS7)	✓
40	25359447	rs182008815			
41	25359352	rs1137188	miR-129-5p, miR-876-5p, miR-421, miR-511, miR-513b, miR-624, miR-541*, miR-1290		
42	25359328	rs1137189	miR-32*, miR-380		✓
43	25359227	rs61764372	miR-365, miR-3121		✓
44	25359217	rs115375135	miR-134, miR-3121		✓
45	25359178	rs188922523	miR-340, miR-132, miR-2052		
46	25358969	rs1137196	miR-129-5p		
47	25358955	rs184169974	miR-129-5p, miR-2115*		
48	25358943	rs8720	miR-2115*		
49	25358890	rs181569153	miR-410, miR-340		
50	25358828	rs12587	miR-425		
51	25358650	rs12245	miR-421, miR-143		
52	25358486	rs189426424	miR-30a,bcde, miR-181abcd, miR-545*		✓
53	25358475	rs14172	miR-181abcd, miR-4262, miR-132		✓
54	25358418	rs61764374	miR-186		
55	25358392	rs192263744	miR-153, miR-448, miR-217, miR-377, miR-570		
56	25358371	rs188034409	miR-570, miR-3157, miR-3148		

Sup. Table 2. All known SNPs in the 3' UTR of *KRAS* and putative miRNA complementary sites

The 3' UTR of *KRAS* contains a total of 56 SNPs reported in dbSNP135. 17 SNPs reside within predicted high confidence miRNA complementary sites, which are putative miRNA complementary sites that are within Argonaute binding sites.

	chr12 (hg19)	Ancestral	Derived	SNP ID	# of DNA sequenced	Freq	% Freq	Putative miRNA complementary sites	LCS	Ago binding
1	25362573	T	G	Novel 1	55	4	7.3	miR-20a*, miR-548X, miR-3148		✓
2	25362552	A	C	rs712	57	43	75.4	miR-422a,,miR-330-5p, miR-3125, miR-877, miR-378bc, miR-1299, miR-193b, miR-200b,c, miR-429	✓	✓
3	25362534	C	T	Novel 2	55	15	27.3	miR-330-5p, miR-326, miR-548d-3p, miR-1299, miR-4314		✓
4	25362532	C	A	Novel 3	55	2	3.6	miR-330-5p, miR-326, miR-548d-3, miR-449c*		
5	25362481	C	T	Novel 4	56	28	50.0	none		
6	25362422	A	C	rs1141947	56	1	1.8	miR-181a,b,c,d, miR-23a,b,miR-377, miR-543, miR-4262		✓
7	25362217	A	G	rs9266	54	37	68.5	miR-181a,b,c,d, miR-4262, miR-132		✓
8	25362033	G	C	Novel 5	57	5	8.8	miR-873, miR-320abcd, miR-5481, miR-4294		✓
9	25361966	G	C	Novel 6	57	4	7.0	miR-380, miR-2054, miR-4323, miR-32*		✓
10	25361950	G	C	Novel 7	54	10	18.5	miR-340, miR-944, miR-126*, miR-4282, miR-32*		✓
11	25361932	A	T	Novel 8	58	3	5.2	miR-335*, miR-944		✓
12	25361888	A	T	Novel 9	55	11	20.0	miR-220c, miR-4270		✓
13	25361863	G	A	Novel 10	58	4	6.9	miR-488, miR-561, miR-1276, miR-2278		✓
14	25361771	C	G	Novel 11	56	6	10.7	miR-193a-3p, miR-193b, miR-328		
15	25361756	C	A	rs61763590	56	4	7.1	miR-133ab, miR-421		
16	25361722	A	G	Novel 12	56	9	16.1	miR-377, miR-320ab, miR-371-5p		
17	25361683	A	G	Novel 13	55	5	9.1	miR-491-5p, miR-128		
18	25361667	C	T	rs61763591	54	1	1.9	miR-200a, miR-141, miR-425, miR-3166		
19	25361649	A	G	Novel 14	54	2	3.7	miR-425, miR-3166		
20	25361646	T	C	rs7960917	54	9	16.7	none		
21	25361645	A	G	Novel 15	54	5	9.3	none		
22	25361621	G	C	Novel 16	50	7	14.0	miR-874		
23	25361142	A	G	rs7973450	55	11	20.0	miR-143, miR-302c*		✓
24	25361091	T	C	rs4597149	55	50	90.9	miR-410, miR-340, miR-376c		✓

25	25361074	G	A	rs7973623	55	9	16.4	miR-501-5p		✓
26	25360559	G	C	rs61764367	61	9	14.8	miR-145*		
27	25360545	T	C	rs61764368	61	1	1.6	miR-630, miR-665,		
28	25360499	G	A	Novel 17	61	38	62.3	miR-335*, miR-25, miR-32, miR-92ab, miR-363, miR-367		
29	25360358	G	A	rs61764369	61	1	1.6	none	✓	
30	25360224	A	C	rs61764370	70	15	21.4	miR-18ab	✓	
31	25360138	T	C	rs4963858	65	64	98.5	miR-599, miR-148a,b, miR-152, miR-199a,b-5p		
32	25359841	T	C	rs13096	64	55	85.9	miR-101, miR-144, miR-493*, let-7a-2*, let-7g*		✓
33	25359577	C	T	rs61764371	60	2	3.3	let-7 family, miR-202	✓	✓
34	25359352	G	A	rs1137188	59	42	71.2	miR-129-5p, miR-876-5p, miR-421, miR-511, miR-513b, miR-624, miR-541*, miR-1290		
35	25359328	A	T	rs1137189	60	31	51.7	miR-380, miR-32*		✓
36	25359320	C	T	Novel 18	61	2	3.3	miR-380, miR-32*		✓
37	25359230	G	A	Novel 19	61	1	1.6	miR-365, miR-24-1*, miR-24-2*, miR-3121		✓
38	25359226	G	A	Novel 20	61	26	42.6	miR-365		✓
39	25359084	T	C	Novel 21	61	2	3.3	miR-143, miR-19ab, miR-524-5p, miR-520d-5p, miR-381, miR-300, miR-3163		
40	25359074	G	T	Novel 22	61	3	4.9	miR-300, miR-381, miR-520d-5p, miR-524-5p, miR-143, miR-3163, miR-551b*		✓
41	25358969	T	C	rs1137196	61	23	37.7	miR-129-5p		
42	25358943	T	C	rs8720	61	45	73.8	none		
43	25358828	T	G	rs12587	64	55	85.9	miR-425		
44	25358650	A	T	rs12245	64	54	84.4	miR-421, miR-143		

Sup. Table 3. The sequence variation identified in our NSCLC cases

A total of 44 sites with sequence variation, which consist of 22 known SNPs and 22 novel variants (or somatic mutations), were identified from sequencing genomic DNA from a maximum 70 lung tumor samples.

A.

	chr12 (hg19)	Ancestral	Derived	SNP ID	Freq	% Freq	Allele frequency (AF) in cases	AF in European	Fold enrichment (Case/Eur)	*p*-value	Putative miRNA complementary sites (microRNA.org and TargetScan)	LCS	Ago binding
1	25362552	A	C	rs712	26	83.9	0.597	0.54	1.11	0.43	miR-422a,miR-330-5p, miR-3125, miR-877, miR-378bc, miR-1299, miR-193b, miR-200bc, miR-429	✓	✓
2	25362465	G	A	rs4285970	31	100.0	1	1	1.00	1.00	501-3p, miR-502-3p,miR-217, miR-4323		
3	25362425	G	A	Novel 1	1	3.2	0.0161	NA	NA	NA	miR-23ab, miR-377, miR-181abcd, miR-4262, miR-543		✓
4	25362217	A	G	rs9266	25	80.6	0.581	0.54	1.08	0.60	miR-181abcd, miR-4262, miR-132		✓
5	25361905	A	G	rs61763589	1	3.2	0.016	0	NA	NA	miR-384, miR-202*, miR-590-3p, miR-580		
6	25361756	C	A	rs61763590	4	12.9	0.081	0.09	0.90	1.00	miR-133ab, miR-421		
7	25361646	T	C	rs7960917	7	22.6	0.113	0.21	0.54	0.07			
8	25361142	A	G	rs7973450	8	25.8	0.129	0.21	0.61	0.14	miR-143, miR-302c*		✓
9	25361091	T	C	rs4597149	31	100.0	1.000	1	1.00	1.00	miR-410, miR-340, miR-376c		✓
10	25361074	G	A	rs7973623	8	25.8	0.129	0.21	0.61	0.14	miR-501-5p		✓
11	25360224	A	C	rs61764370	6	19.4	0.097	0.09	1.08	0.82	miR-18a,b	✓	
12	25360138	T	C	rs4963858	31	100.0	1.000	1	1.00	1.00	miR-599, miR-148a,b, miR-152, miR-199a,b-5p		
13	25359898	A	G	rs191137453	1	3.2	0.016	0	NA	NA	miR-26a,b		
14	25359841	T	C	rs13096	24	77.4	0.565	0.54	1.05	0.79	miR-101, miR-144, miR-493*, let-7a-2*, let-7g*		✓
15	25359577	C	T	rs61764371	2	6.5	0.032	0	NA	NA	let-7 family, miR-202	✓	✓
16	25359352	G	A	rs1137188	25	80.6	0.581	0.54	1.08	0.60	miR-129-5p, miR-876-5p, miR-421, miR-511, miR-513b, miR-624, miR-541*, miR-1290		

17	25359328	A	T	rs1137189	26	83.9	0.597	0.54	1.11	0.43	miR-32*, miR-380		✓
18	25358969	T	G	rs1137196	24	77.4	0.516	0.44	1.17	0.29	miR-129-5p		
19	25358943	T	C	rs8720	25	80.6	0.581	0.54	1.08	0.60	miR-2115*		
20	25358828	T	G	rs12587	26	83.9	0.597	0.54	1.11	0.43	miR-425		
21	25358650	A	T	rs12245	16	51.6	0.435	0.54	0.81	0.14	miR-421, miR-143		
22	25358418	T	C	rs61764374	1	3.2	0.016	0.05	0.32	0.35	miR-186		

B.

	Hg19	Ancestral	Derived	SNP ID	Frequency	% Frequency	Allele frequency (AF) by SAMtools	AF by GATK
1	25360449	C	A	Novel 2	12	38.7	0.1935	Identified as an indel
2	25360447	A	C	Novel 3	4	12.9	0.0645	Not identified
3	25359466	A	C	Novel 4	3	9.7	0.0484	Not identified
4	25359465	A	T	Novel 5	3	9.7	0.0484	Not identified
5	25358670	T	C	Novel 6	2	6.5	0.0323	Not identified
6	25358669	T	C	Novel 7	5	16.1	0.0806	Not identified
7	25358664	T	C	Novel 8	2	6.5	0.0323	Not identified

Sup. Table 4. The sequence variation identified in our 31 EOC cases

A. A total of 22 sites with sequence variation, which consist of 21 known SNPs and 1 novel variant, were identified from sequencing germline DNA. To measure fold enrichment, allele frequency of derived allele at each varying site was compared between our cases and European controls reported in the 1000 Genomes Project. B. 7 novel variants were identified by SAMtools only.

	chr12 (hg19)	Ancestral	Derived	SNP ID	% Freq of NSCLC cases with the derived allele	Derived allele frequency in EOC cases	Putative miRNA complementary sites	LCS	Ago binding

1	25362552	A	C	rs712	75.4	0.597	miR-422a,miR-330-5p, miR-3125, miR-877, miR-378bc, miR-1299, miR-193b, miR-200b,c, miR-429	✓	✓
2	25362465	G	A	rs4285970	N/A	1	501-3p, miR-502-3p,miR-217, miR-4323		
3	25362422	A	C	rs1141947	1.8	N/A	miR-181a,b,c,d, miR-23a,b,miR-377, miR-543, miR-4262		✓
4	25362217	A	G	rs9266	68.5	0.581	miR-181a,b,c,d, miR-4262, miR-132		✓
5	25361905	A	G	rs61763589	N/A	0.016	miR-384, miR-202*, miR-590-3p, miR-580		
6	25361756	C	A	rs61763590	7.1	0.081	miR-133ab, miR-421		
7	25361667	C	T	rs61763591	1.9	N/A	miR-200a, miR-141, miR-425, miR-3166		
8	25361646	T	C	rs7960917	16.7	0.113	none		
9	25361142	A	G	rs7973450	20	0.129	miR-143, miR-302c*		✓
10	25361091	T	C	rs4597149	90.9	1	miR-410, miR-340, miR-376c		✓
11	25361074	G	A	rs7973623	16.4	0.129	miR-501-5p		✓
12	25360559	G	C	rs61764367	14.8	N/A	miR-145*		
13	25360545	T	C	rs61764368	1.6	N/A	miR-630, miR-665,		
14	25360358	G	A	rs61764369	1.6	N/A	none	✓	
15	25360224	A	C	rs61764370	21.4	0.097	miR-18ab	✓	
16	25360138	T	C	rs4963858	98.5	1	miR-599, miR-148a,b, miR-152, miR-199a,b-5p		
17	25359898	A	G	rs191137453	N/A	0.016	miR-26a,b		
18	25359841	T	C	rs13096	85.9	0.565	miR-101, miR-144, miR-493*, let-7a-		✓

18	25359841	T	C	rs13096	85.9	0.565	miR-101, miR-144, miR-493*, let-7a-2*, let-7g*		✓
19	25359577	C	T	rs61764371	3.3	0.032	let-7 family, miR-202	✓	✓
20	25359352	G	A	rs1137188	71.2	0.581	miR-129-5p, miR-876-5p, miR-421, miR-511, miR-513b, miR-624, miR-541*, miR-1290		
21	25359328	A	T	rs1137189	51.7	0.597	miR-380, miR-32*		✓
22	25358969	T	C	rs1137196	37.7	0.516	miR-129-5p		
23	25358943	T	C	rs8720	73.8	0.581	none		
24	25358828	T	G	rs12587	85.9	0.597	miR-425		
25	25358650	A	T	rs12245	84.4	0.435	miR-421, miR-143		

Sup. Table 5. The union of known SNPs identified in both NSCLC and EOC cases

A total of 26 known SNPs were identified in our NSCLC and EOC cases. LCS: *let-7* complementary site

	Available for known	miRNA complementary sites predicted by the Miranda algorithm with a default	

					SNPs				setting					
					Patrocles (8mer)		miRNASNP (default setting)							
	Chr12 hg19	Ancetral	Derived	SNP ID	Gain	Loss	Gain	Loss	Target sequence used	With the ancestral allele	With the derived allele	Gain with the derived allele	Loss with the derived allele	lost high confidence miR complementary sites with SNP
1	25362573	T	G	Novel 1					TTAAATGCTTATTTTAAAATGACaGTGGAAGTTTTTTTTTCCTCtAAG	miR-4668-5p,miR-548ae,miR-548ah-3p,miR-548aq-3p,miR-548x-3p,miR-3916,miR-548aj-3p,miR-3613-3p,miR-3148,miR-548am-3p,miR-5582-3p	miR-4668-5p,miR-1323,miR-548ae,miR-548ah-3p,miR-548aq-3p,miR-548x-3p,miR-3916,miR-548aj-3p,miR-3613-3p,miR-3148,miR-548am-3p,miR-5582-3p	miR-1323		
2	25362552	A	C	rs712	none	none		miR-877, miR-3125	CAGTGGAAGTTTTTTTTTCCTCtAAGTGCCAGTATTCCCAGAGTTT	miR-200c-3p,miR-429,miR-330-5p,miR-3125,miR-3915,miR-514a-5p,miR-3916,miR-378c,miR-5588-5p,miR-200b-3p,miR-4646-5p,miR-877-5p	miR-200c-3p,miR-429,miR-330-5p,miR-3915,miR-514a-5p,miR-3916,miR-516a-5p,miR-200b-3p,miR-4646-5p	miR-516a-5p	miR-3125, miR-378c,miR-5588-5p,miR-877-5p,miR-514a-5p	miR-378, miR-3125, miR-877
3	25362534	C	T	Novel 2					TCCTCTAAGTGCCAGTATTCCCAgAGTTTTGGTTTTTGAACTAGCA	miR-4314,miR-548d-3p,miR-4432,miR-548h-3p,miR-548t-3p,miR-1323,miR-548aa,miR-330-5p,miR-548ap-3p,miR-548ac,miR-514a-5p,miR-548o-3p,miR-204-3p,miR-4646-5p,miR-548z,miR-326	miR-548d-3p,miR-548h-3p,miR-548t-3p,miR-1323,miR-548aa,miR-548ap-3p,miR-450a-3p,miR-548ac,miR-548o-3p,miR-561-5p,miR-548z,miR-5582-3p	miR-450a-3p,miR-561-5p,miR-5582-3p	miR-4314,miR-4432,miR-330-5p,miR-514a-5p,miR-204-3p,miR-4646-5p,miR-326	miR-4314, miR-326

4	25362532	C	A	Novel3					CTCtAAGTGCCAGTATTCCCAGAgTTTTGGTTTTTGAACTAGCAAT	miR-4314,miR-548d-3p,miR-4432,miR-548h-3p,miR-548t-3p,miR-1323,miR-548aa,miR-330-5p,miR-548ap-3p,miR-548ac,miR-514a-5p,miR-548o-3p,miR-449c-3p,miR-548z,miR-326	miR-4314,miR-548d-3p,miR-548h-3p,miR-548t-3p,miR-548aa,miR-548ap-3p,miR-548ac,miR-449c-3p,miR-3156-5p,miR-548c-3p,miR-548z	miR-548c-3p,miR-3156-5p	miR-4432,miR-1323,miR-330-5p,miR-514a-5p,miR-548o-3p,miR-326	
5	25362481	C	T	Novel4					GAAAAAGAAACTGAATACCTAAgATTTCTGTCTTGGGGTTTTTGGT	miR-548d-3p,miR-548h-3p,miR-590-3p,miR-652-5p,miR-1324,miR-4662a-3p,miR-5695,miR-548c-3p,miR-548z,miR-548as-3p	miR-548d-3p,miR-548h-3p,miR-590-3p,miR-652-5p,miR-1324,miR-4662a-3p,miR-5695,miR-548c-3p,miR-548z,miR-4775,miR-548as-3p	miR-4775		
6	25362422	A	C	rs1141947	none	none	miR-3614-5p		TTACTTCTTATTTTTCTTACCAAtTGTGAATGTTGGTGTGAAACAA	miR-1179,miR-3692-3p,miR-543,miR-181d,miR-181c-5p,miR-27a-3p,miR-181b-5p,miR-4262,miR-4490,miR-181a-5p,miR-27b-3p	miR-1179,miR-342-3p,miR-543,miR-3591-3p,miR-3614-5p,miR-181d,miR-181c-5p,miR-181b-5p,miR-4262,miR-4490,miR-181a-5p	miR-342-3p,miR-3591-3p,miR-3614-5p	miR-3692-3p,miR-27a-3p,miR-27b-3p	
7	25362217	A	G	rs9266	none	none			TCCTATAGTTTGTCATCCCTGAtGAATGTAAAGTTACACTGTTCAC	miR-181d,miR-181c-5p,miR-181b-5p,miR-4262,miR-4518,miR-181a-5p	miR-4518,miR-4775	miR-4775	miR-181abcd,miR-4518	miR-181, miR-4262
8	25362033	G	C	Novel5					AGATAAATTACTATAAAGACTCcTAATAGCTTTTCCTGTTAAGGCA	miR-3153,miR-548x-5p,miR-548aj-5p,miR-302d-5p,miR-548at-5p,miR-924,miR-548g-5p,miR-4294	miR-3153,miR-548x-5p,miR-548aj-5p,miR-302d-5p,miR-548at-5p,miR-924,miR-548g-5p		miR-4294	miR-4294
9	25361966	G	C	Novel6					TTATTATAGCAACCATTTTGGGGcTATATTTACATGCTACTAAATT	miR-4323,miR-3668,miR-3651,miR-4495,miR-32-3p,miR-3935,miR-16-5p	miR-4460,miR-4495,miR-32-3p,miR-16-5p	miR-4460	miR-4323,miR-3668,miR-3651,miR-3935	miR-4323
10	25361950	G	C	Novel7					TTGGGGcTATATTTACATGCTAcTAAATTTTTATAATAATTGAAAA	,miR-4282,miR-126-5p,miR-944,miR-32-3p,miR-16-5p	miR-4282,miR-126-5p,miR-944,miR-32-3p,miR-16-5p			

11	25361932	A	T	Novel8					TGCTACTAAATTTTTATAATAATtGAAAAGATTTTAACAAGTATAA	miR-126-5p,miR-944,miR-548c-3p	miR-126-5p,miR-944,miR-548c-3p			
12	25361888	A	T	Novel9					AAAAAATTCTCATAGGAATTAAAtGTAGTCTCCCTGTGTCAGACTG	miR-4270,miR-4441	miR-4270,miR-4441			
13	25361863	G	A	Novel10					TAGTCTCCCTGTGTCAGACTGCTcTTTCATAGTATAACTTTAAATC	miR-1276,miR-2278,miR-4274,miR-548at-5p,miR-4712-3p,miR-4766-5p,miR-4670-3p	miR-4274,miR-3185,miR-3688-3p,miR-548at-5p,miR-4670-3p	miR-3185,miR-3688-3p	miR-1276,miR-2278,miR-4712-3p,miR-4766-5p	miR-1276,miR-2278
14	25361771	C	G	Novel11					ACATTAAAAGATTATTTGGGCCAgTTATAGCTTATTAGGTGTTGAA	miR-3161,miR-193b-3p,miR-3065-3p	miR-3677-5p,miR-3161,miR-4795-5p,miR-663b,miR-3545-5p,miR-5693	miR-3677-5p,miR-4795-5p,miR-663b,miR-3545-5p,miR-5693	miR-193b-3p,miR-3065-3p,miR-193a-3p	miR-193a*
15	25361756	C	A	rs61763590					TTGGGCCAGTTATAGCTTATTAGgTGTTGAAGAGACCAAGGTTGCA	miR-5002-5p,miR-3065-3p,miR-1305,miR-676-5p	miR-5583-5p,miR-549,miR-1305,miR-676-5p,miR-3129-3p	miR-5583-5p,miR-549,miR-3129-3p	miR-5002-5p,miR-3065-3p	
16	25361722	A	G	Novel12					ACCAAGGTTGCAAGGCCAGGCCCtGTGTGAACCTTTGAGCTTTCAT	miR-557,miR-485-3p,miR-3918,miR-4512,miR-2861,miR-3158-3p,miR-377-3p	miR-557,miR-744-5p,miR-4717-3p,miR-4462,miR-2861,miR-602	miR-744-5p,miR-4717-3p,miR-4462,miR-602	miR-485-3p,miR-3918,miR-4512,miR-3158-3p,miR-377-3p	miR-377

17	25361683	A	G	Novel13					CTTTCATAGAGAGTTTCACAGCAtGGACTGTGTCCCCACGGTCATC	miR-3691-5p,miR-491-5p,miR-141-3p,miR-450a-3p,miR-200a-3p,miR-549,miR-4504,miR-1243,miR-4318	miR-937,miR-491-5p,miR-4700-5p,miR-4693-5p	miR-937,miR-4700-5p	miR-450a-3p,miR-455-3p,miR-5581-3p,miR-1302	
18	25361667	C	T	rs61763591			miR-943		CACAGCATGGACTGTGTCCCCACgGTCATCCAGTGTTGTCAtGCAT	miR-3691-5p,miR-491-5p,miR-141-3p,miR-450a-3p,miR-200a-3p,miR-549,miR-4504,miR-1243,miR-4318	miR-3691-5p,miR-491-5p,miR-141-3p,miR-450a-3p,miR-200a-3p,miR-549,miR-4504,miR-1243,miR-4318			
19	25361649	A	G	Novel14					CCCACGGTCATCCAGTGTTGTCAtGCATTGGTTAGTCAAAATGGGG	miR-148b-3p,miR-152,miR-136-5p,miR-5700,miR-4504,miR-148a-3p	miR-136-5p,miR-542-3p,miR-4504	miR-542-3p,miR-4504	miR-148b-3p,miR-152,miR-5700,miR-148a-3p	
20	25361646	T	C	rs7960917			miR-3912		ACGGTCATCCAGTGTTGTCATGCaTTGGTTAGTCAAAATGGGGAGG	miR-148b-3p,miR-152,miR-136-5p,miR-5700,miR-148a-3p	miR-3912,miR-152,miR-5700	miR-3912	miR-148b-3p,miR-136-5p,miR-148a-3p	
21	25361645	A	G	Novel15					CGGTCATCCAGTGTTGTCAtGCATTGGTTAGTCAAAATGGGGAGGG	miR-148b-3p,miR-152,miR-136-5p,miR-5700,miR-148a-3p	miR-148b-3p,miR-152,miR-2052,miR-199b-5p,miR-1825,miR-148a-3p,miR-4676-5p,miR-3136-5p	miR-2052,miR-199b-5p,miR-1825,miR-4676-5p,miR-3136-5p	miR-136-5p,miR-5700	
22	25361621	G	C	Novel16					TGGTTAGTCAAAATGGGGAGGGAcTAGGGCAGTTTGGATAGCTCAA	miR-3157-3p,miR-554,miR-18a-3p,miR-2114-5p,miR-548av-3p,miR-642a-5p,miR-4769-3p	miR-4685-3p,miR-3157-3p,miR-18a-3p,miR-4469,miR-550b-3p,miR-4290,miR-548av-3p,miR-642a-5p,miR-4769-3p	miR-4685-3p,miR-4469,miR-550b-	miR-554,miR-2114-5p	

												3p,miR-4290		
23	25361142	A	G	rs7973450	none	none			ATCACTTACTATCCATTTCTTCAtGTTAAAAGAAGTCATCTCAAAC	miR-302c-5p,miR-302b-5p,miR-143-3p,miR-4517,miR-3915,miR-135a-5p,miR-302d-5p	miR-302b-5p,miR-143-3p,miR-3915,miR-3611,miR-29a-5p,miR-302d-5p	miR-3611,miR-29a-5p	miR-302c-5p,miR-4517,miR-135a-5p	
24	25361091	T	C	rs4597149					GTTTTTTTTTTTTACAACTATGTaATTTATATTCCATTTACATAAG	miR-1,miR-224-5p,miR-3673,miR-4694-3p,miR-4495	miR-1,miR-224-5p,miR-3673,miR-4694-3p,miR-4495			
25	25361074	G	A	rs7973623					CTATGTAATTTATATTCCATTTAcATAAGGATACACTTATTTGTCA	miR-595,miR-4495	miR-519b-3p,miR-519a-3p,miR-519c-3p,miR-568	miR-519abc-3p,miR-568	miR-595,miR-4495	
26	25360559	G	C,A	rs61764367			miR-323-3p		GCTGAAAGAATTCCTTAGGTAATcTATAACTAGGACTACTCCTGGT	miR-3545-5p,miR-4540,miR-409-5p,miR-3674	miR-4317,miR-3545-5p,miR-4540,miR-323a-3p	miR-4317,miR-323a-3p	miR-409-5p,miR-3674	
27	25360545	T	C	rs61764368			miR-1910,miR4274		TTAGGTAATCTATAACTAGGACTaCTCCTGGTAACAGTAATACATT	miR-665,miR-3545-5p,miR-4540,miR-4433-3p	miR-665,miR-4274,miR-1910,miR-4540	miR-4274,miR-1910	miR-3545-5p,miR-4433-3p	
28	25360499	G	A	Novel17					CCATTGTTTTAGTAACCAGAAATcTTCATGCAATGAAAAATACTTT	miR-3149,miR-876-5p,miR-335-3p,miR-4699-5p	miR-513a-3p,miR-3149,miR-4282,miR-335-3p,miR-513c-3p	miR-513a-3p,miR-4282,miR-513c-3p	miR-876-5p,miR-4699-5p	
29	25360358	G	A	rs61764369					CCATCTCCCAGGTTCAAGCGATTcTCGTGCCTCGGCCTCCtGAGTA	miR-3622a-5p,miR-4459,miR-485-5p,miR-510,miR-3664-3p,miR-4695-5p	miR-3622a-5p,miR-4459,miR-485-5p,miR-510,miR-3664-3p,miR-3929,miR-4695-5p	miR-3929	none	

30	25360224	A	C	rs61764370				miR-34b, miR-1262	TCGAACTCCTGACCTCAAGTGATtCACCCACCTTGGCCTCATAAAC	miR-4761-5p,miR-34b-3p,miR-1262,miR-363-5p,miR-4701-3p	miR-4761-5p		miR-34b-3p,miR-1262,miR-363-5p,miR-4701-3p	
31	25360138	T	C	rs4963858	miR-147b	none	miR-147b	miR-147, miR-581	GTGCCTACCAGATGCCAGTCACCgCACAAGGCACTGGGTATATGGT	miR-4312,miR-147b,miR-3130-5p,miR-4482-5p,miR-515-3p,miR-1825,miR-519e-3p,miR-33b-3p	miR-4312,miR-1294,miR-3130-5p,miR-4482-5p,miR-4783-3p,miR-515-3p,miR-1825,miR-519e-3p,miR-33b-3p	miR-1294	miR-147b	
32	25359841	T	C	rs13096				miR-2355-3p, miR-676	TTTGGCATAACTGTGATTCTTTTaGGACAATTACTGTACACATTAA	let-7g-3p,miR-2355-3p,miR-676-3p,miR-219-5p,miR-1244,miR-3177-5p,let-7a-2-3p,miR-4766-5p	let-7g-3p,miR-219-5p,miR-1244,miR-4646-3p,miR-548x-5p,miR-548aj-5p,miR-3177-5p,let-7a-2-3p,miR-548g-5p	miR-4646-3p,miR-548x-5p,miR-548aj-5p,miR-548g-5p	miR-2355-3p,miR-676-3p,miR-4766-5p	
33	25359577	C	T	rs61764371					TGTTAAGACTTACACAGTACCTCGTTTCTACACAGAGAAAGAAATG	miR-147a	miR-5680,miR-143-3p,miR-147a,miR-5093	miR-5680,miR-143-3p,miR-5093		
34	25359352	G	A	rs1137188	none	none			TGTTAAGACTTACACAGTACCTCGTTTCTACACAGAGAAAGAAATG	miR-541-5p,miR-511,miR-302b-5p,miR-548u,miR-548ah-3p,miR-548aq-3p,miR-1290,miR-676-5p,miR-302d-5p,miR-561-5p,miR-548am-3p	miR-541-5p,miR-302b-5p,miR-548u,miR-548ah-3p,miR-548aq-3p,miR-1290,miR-676-5p,miR-302d-5p,miR-561-5p,miR-548am-3p		miR-511	miR-511
35	25359328	A	T	rs1137189					AAAAATCCTTGTTGAAGTTTTTTtAAAAAAAGCTAAATTACATAGA	miR-3658,miR-380-3p,miR-32-3p	miR-3658,miR-380-3p,miR-32-3p,miR-2054	miR-2054		
36	25359320	C	T	Novel18					TTGTTGAAGTTTTTTTAAAAAAAgCTAAATTACATAGACTTAGGCA	miR-380-3p,miR-32-3p	miR-5002-5p,miR-380-3p,miR-32-3p	miR-5002-5p		

37	25359230	G	A	Novel19					GTTCCCAAGTAGGCATTcTAGGCTCTATTTAACTGAGTCACACTGC	miR-24-1-5p,miR-3673,miR-515-3p,miR-3116,miR-3121-3p,miR-934,miR-24-2-5p	miR-3116,miR-3121-3p		miR-24-1-5p,miR-3673,miR-515-3p,miR-934,miR-24-2-5p	miR-24
38	25359226	G	A	Novel20					AGGCTCTATTTAACTGAGTCACACTGCATAGGAATTTAGAACCTAA	miR-3673,miR-515-3p,miR-3116,miR-3121-3p	miR-17-5p,miR-20a-5p,miR-106a-5p,miR-519d,miR-515-3p,miR-526b-3p,miR-4427,miR-3121-3p	miR-17-5p,miR-20a-5p,miR-106a-5p,miR-519d,miR-526b-3p,miR-4427	miR-3673,miR-3116	
39	25359084	T	C	Novel21					GGGCATGTTAAGTTACAGTTTGCaCAAGTTCATCTCATTTGTATTC	miR-19a-3p,miR-1273f,miR-19b-3p,miR-143-3p,miR-5009-5p,miR-4771,miR-4770	miR-143-3p,let-7i-3p,miR-5009-5p,miR-4771,miR-4770	let-7i-3p	miR-19ab-3p,miR-1273f	miR-19ab
40	25359074	G	T	Novel22					AGTTACAGTTTGCACAAGTTCATcTCATTTGTATTCCATTGATTTT	miR-551b-5p,miR-1273f,miR-143-3p,miR-4770			miR-551b-5p,miR-1273f,miR-143-3p,miR-4770	miR-551b, miR-143
41	25358969	T	C	rs1137196					TTTAGACAGCAAAAACTATCTGAaGATTTCCATTTGTCAAAAAGTA	miR-3942-3p,miR-3688-3p,miR-4694-3p,miR-5683,miR-182-5p	miR-4330,miR-3688-3p,miR-4694-3p,miR-5683,miR-182-5p,miR-4668-3p	miR-4330,miR-4668-3p	miR-3942-3p	
42	25358943	T	C	rs8720			miR-885-5p		TTTCCATTTGTCAAAAAGTAATGaTTTCTTGATAATTGTGTAGTAA	miR-126-5p,miR-539-5p,miR-15b-3p,miR-561-5p	miR-885-5p,miR-548t-3p,miR-548a,miR-451a,miR-561-5p,miR-451b	miR-885-5p,miR-548t-3p,miR-548aa,	miR-126-5p,miR-539-5p,miR-15b-3p	

												miR-451a,miR-451b		
43	25358828	T	G	rs12587					TAGCATGAATTCTGCATTGAGAAaCTGAATAGCTGTCATAAAATGA	miR-223-3p	miR-657,miR-506-5p	miR-657	miR-506-5p, miR-223-3p	
44	25358650	A	T	rs12245	none	none	miR-544		GGGAAAAAAAAAGTTATCTGCAGAtATGTTGAGGGCCCATCTCTCCC	miR-1277-5p,miR-654-5p,miR-4644	miR-654-5p,miR-4644,miR-3143,miR-16-2-3p,miR-544a	miR-3143,miR-16-2-3p,miR-544a	miR-1277-5p	

Sup. Table 6. The effects of variants identified in NSCLC cases on putative miRNA complementary sites

Patrocles with an 8-mer setting, and miRNASNP with a default setting were utilized. Target sequences including alternative alleles were used to predict gain or loss of miRNA complementary sites by the derived allele using the miRanda algorithm with a default setting.

					Only available for known SNPs									
					Patrocles (8mer)		mirnasnp		miRNA complementary sites predicted by the Miranda algorithm with a default setting					
	Chr12 hg19	Ancetral	Derived	SNP ID	Gain	Loss	Gain	Loss	Target sequence used	With the ancestral allele	With the SNP allele	Gain with SNP	Loss with SNP	lost high confidence miR complementary sites with SNP
1	25362552	A	C	rs712	none	none		miR-877, miR-3125	CaGTGGAAGTTTTTTTTTCCTCtAAGTGCCAGTATTCCCAgAgTTT	miR-200c-3p,miR-429,miR-330-5p,miR-3125,miR-3915,miR-514a-5p,miR-3916,miR-378c,miR-5588-5p,miR-200b-3p,miR-4646-5p,miR-877-5p	miR-200c-3p,miR-429,miR-330-5p,miR-3915,miR-514a-5p,miR-3916,miR-516a-5p,miR-200b-3p,miR-4646-5p	miR-516a-5p	miR-3125,miR-378c,miR-5588-5p,miR-877-5p,miR-514a-5p	miR-378, miR-3125, miR-877
2	25362465	G	A	rs4285970			miR-548z	miR-4323	ATACCTAAgATTTCTGTCTTGGGGcTTTTGGTGCATGCAGTTGATTACT	miR-4323,miR-502-3p,miR-217,miR-335-5p,miR-5695,miR-5689,miR-501-3p	miR-548d-3p,miR-548h-3p,miR-652-5p,miR-548ac,miR-502-3p,miR-217,miR-5695,miR-548c-3p,miR-548z,miR-501-3p,miR-548as-3p	miR-548d-3p,miR-548h-3p,miR-652-5p,miR-548ac,miR-548c-3p,miR-548z,miR-548as-3p	miR-4323,miR-335-5p,miR-5689	miR-502-3p,miR-4323
3	25362425	G	A	Novel 1					TTGATTACTTCTTATTTTTCTTACcAAtTGTGAATGTTGGTGTGAAACA	miR-1179,miR-543,miR-181d,miR-181c-5p,miR-27a-3p,miR-181b-5p,miR-4262,miR-4490,miR-181a-5p,miR-27b-3p	miR-543,miR-181d,miR-181c-5p,miR-181b-5p,miR-4262,miR-181a-5p,miR-921	miR-921	miR-1179,miR-27a-3p,miR-4490,miR-27b-3p	
4	25362217	A	G	rs9266	none	none			TCCTATAGTTTGTCATCCCTGAtGAATGTAAAGTTACACTGT	miR-181d,miR-181c-5p,miR-181b-5p,miR-4262,miR-4518,miR-181a-5p	miR-4518,miR-4775	miR-4775	miR-181abcd,miR-4518	miR-181, miR-4262

									TCAC					
5	25361905	A	G	rs61763589				miR-580	AAAGATTTTAACAAGTATAAAAAAtTCTCATAGGAATTAAAtGTAGTCT	miR-202-5p,miR-580,miR-3123,miR-4775	miR-202-5p,miR-4712-3p	miR-4712-3p	miR-580,miR-3123,miR-4775	miR-384, miR-590-3p, miR-582
6	25361756	C	A	rs61763590					TTGGGCCAgTTATAGCTTATTAGgTGTTGAAGAGACCAAGGTTGCA	miR-5002-5p,miR-3065-3p,miR-1305,miR-676-5p	miR-5583-5p,miR-549,miR-1305,miR-676-5p,miR-3129-3p	miR-5583-5p,miR-549,miR-3129-3p	miR-5002-5p,miR-3065-3p	
7	25361646	T	C	rs7960917			miR-3912		ACgGTCATCCAGTGTTGTCAtGCatTGGTTAGTCAAAATGGGGAGG	miR-148b-3p,miR-152,miR-136-5p,miR-5700,miR-148a-3p	miR-3912,miR-152,miR-5700	miR-3912	miR-148b-3p,miR-136-5p,miR-148a-3p	
8	25361142	A	G	rs7973450	none	none			ATCACTTACTATCCATTTCTTCAtGTTAAAAGAAGTCATCTCAAAC	miR-302c-5p,miR-302b-5p,miR-143-3p,miR-4517,miR-3915,miR-135a-5p,miR-302d-5p	miR-302b-5p,miR-143-3p,miR-3915,miR-3611,miR-29a-5p,miR-302d-5p	miR-3611,miR-29a-5p	miR-302c-5p,miR-4517,miR-135a-5p	
9	25361091	T	C	rs4597149					gTTTTTTTTTTTTACAACTATGTaATTTATATTCCATTTAcATAAG	miR-1,miR-224-5p,miR-3673,miR-4694-3p,miR-4495	miR-1,miR-224-5p,miR-3673,miR-4694-3p,miR-4495			
10	25361074	G	A	rs7973623					CTATGTaATTTATATTCCATTTAcATAAGGATACACTTATTTGTCA	miR-595,miR-4495	miR-519b-3p,miR-519a-3p,miR-519c-3p,miR-568	miR-519abc-3p,miR-568	miR-595,miR-4495	
11	25360449	C	A	Novel 2					TCATGAAGCTTAcTTTTTTTTTTgGtGTCAGAGTCTCGCTCTTGTCAC	miR-3672, miR-4431, miR-4714-5p, miR-301a-5p, miR-4522, miR-335-5p, miR-4801	none	none	miR-3672, miR-4431, miR-4714-5p, miR-301a-5p, miR-4522,	miR-335

													miR-335-5p, miR-4801	
12	25360447	A	C	Novel 3					ATGAAGCTTAcTTTTTTTTTTgGtGTCAGAGTCTCGCTCTTGTCACCC	miR-4431,miR-4714-5p,miR-301a-5p,miR-1273a,miR-4522,miR-335-5p	miR-4431,miR-4714-5p,miR-301a-5p,miR-4256, miR-1273a,miR-4522,miR-335-5p	miR-4256		
13	25360224	A	C	rs61764370				miR-34b, miR-1262	TCGAACTCCTGACCTCAAGTGATtCACCCACCTTGGCCTCATAAAC	miR-4761-5p,miR-34b-3p,miR-1262,miR-363-5p,miR-4701-3p	miR-4761-5p		miR-34b-3p,miR-1262,miR-363-5p,miR-4701-3p	
14	25360138	T	C	rs4963858	miR-147b	none	miR-147b	miR-147, miR-581	GTGCCTACCAGATGCCAGTCACCgCACAAGGCACTGGGTATATGGT	miR-4312,miR-147b,miR-3130-5p,miR-4482-5p,miR-515-3p,miR-1825,miR-519e-3p,miR-33b-3p	miR-4312,miR-1294,miR-3130-5p,miR-4482-5p,miR-4783-3p,miR-515-3p,miR-1825,miR-519e-3p,miR-33b-3p	miR-1294	miR-147b (used c as wt)	
15	25359898	A	G	rs191137453				miR-2355-3p, miR-676	CTTTATGTAAATCACTTCATTGTTtTAAAGGAATAAACTTGATTATATT	miR-561-3p	none	miR-561-3p		
16	25359841	T	C	rs13096				miR-2355-3p, miR-677	TTTGGCATAACTGTGATTCTTTTaGGACAATTACTGTACACATTAA	let-7g-3p,miR-2355-3p,miR-676-3p,miR-219-5p,miR-1244,miR-3177-5p,let-7a-2-3p,miR-4766-5p	let-7g-3p,miR-219-5p,miR-1244,miR-4646-3p,miR-548x-5p,miR-548aj-5p,miR-3177-5p,let-7a-2-3p,miR-548g-5p	miR-4646-3p,miR-548x-5p,miR-548aj-5p,miR-548g-5p	miR-2355-3p,miR-676-3p,miR-4766-5p	
17	25359577	C	T	rs61764371					TGTTAAGACTTACACAGTACCTCGTTTCTACACAGAGAAA	miR-147a	miR-5680,miR-143-3p,miR-147a,miR-5093	miR-5680,miR-143-3p,miR-5093		

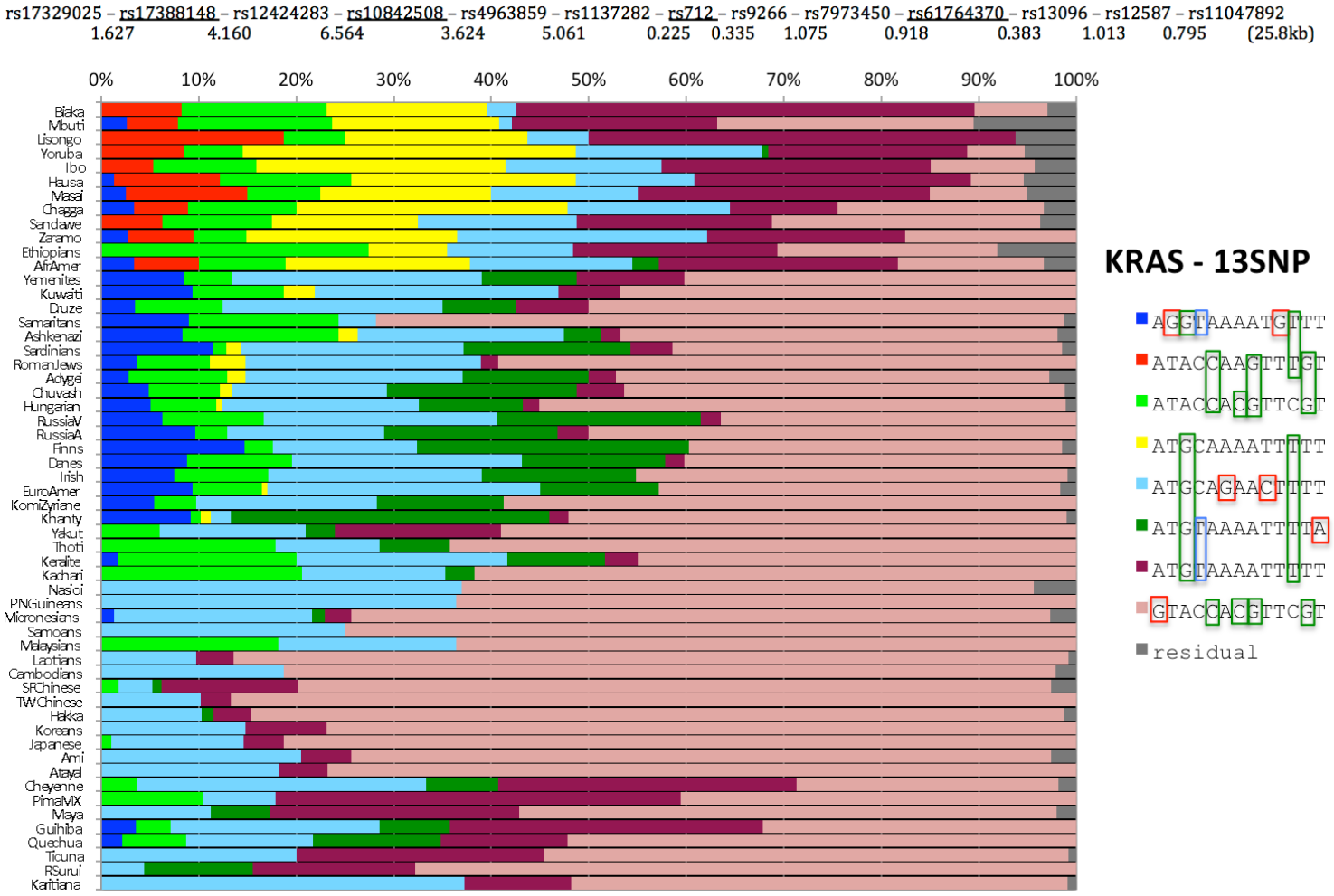
									GAAATG					
18	25359466	A	C	Novel 4					ATGGGCATTTTTTTAAGGTAGTGGtTAATTACCTTTATGTGAACTTTGA	miR-548ag,miR-570-5p,miR-376c,miR-548m,miR-548ai	miR-548ag,miR-570-5p,miR-376c,miR-548m,miR-548ai,miR-196b-5p,miR-4301	miR-196b-5p,miR-4301		
19	25359465	A	T	Novel 5					TGGGCATTTTTTTAAGGTAGTGGTtAATTACCTTTATGTGAACTTTGAA	miR-2681-5p,miR-548ag,miR-570-5p,miR-376c,miR-548m,miR-196b-5p,miR-377-3p,miR-548ai	none		miR-2681-5p,miR-548ag,miR-570-5p,miR-376c,miR-548m,miR-196b-5p,miR-377-3p,miR-548ai	miR-548m
20	25359352	G	A	rs1137188	none	none		miR-511	TGTTAAGACTTACACAGTACCTCGTTTCTACACAGAGAAAGAAATG	miR-541-5p,miR-511,miR-302b-5p,miR-548u,miR-548ah-3p,miR-548aq-3p,miR-1290,miR-676-5p,miR-302d-5p,miR-561-5p,miR-548am-3p	miR-541-5p,miR-302b-5p,miR-548u,miR-548ah-3p,miR-548aq-3p,miR-1290,miR-676-5p,miR-302d-5p,miR-561-5p,miR-548am-3p		miR-511	miR-511
21	25359328	A	T	rs1137189					AAAAATCCTTGTTGAAGTTTTTTtAAAAAAgCTAAATTACATAGA	miR-3658,miR-380-3p,miR-32-3p	miR-3658,miR-380-3p,miR-32-3p,miR-2054	miR-2054		
22	25358969	T	G	rs1137196					TTTAGACAGCAAAAACTATCTGAaGATTTCCATTTGTCAAAAAGTA	miR-3942-3p,miR-3688-3p,miR-4694-3p,miR-5683,miR-182-5p	miR-4330,miR-3688-3p,miR-4694-3p,miR-5683,miR-182-5p,miR-4668-3p	miR-4330,miR-4668-3p	miR-3942-3p	

23	25358943	T	C	rs8720			miR-885-5p		TTTCCATTTGTCAAAAAGTAATGaTTTCTTGATAATTGTGTAGTAA	miR-126-5p,miR-539-5p,miR-15b-3p,miR-561-5p	miR-885-5p,miR-548t-3p,miR-548a,miR-451a,miR-561-5p,miR-451b	miR-885-5p,miR-548t-3p,miR-548aa,miR-451a,miR-451b	miR-126-5p,miR-539-5p,miR-15b-3p	
24	25358828	T	G	rs12587					TAGCATGAATTCTGCATTGAGAAaCTGAATAGCTGTCATAAAATGA	miR-223-3p	miR-657,miR-506-5p	miR-657	miR-506-5p, miR-223-3p	
25	25358670	T	C	Novel 6					AGGTAATTTAGATGAATTTAGGGGaaAAAAaAGTTATCTGCAGAtATGT	miR-5195-5p,miR-3158-5p,miR-135a-5p,miR-4775	miR-5195-5p,miR-3158-5p,miR-135a-5p,miR-4776,miR-3679-3p,miR-642a-5p	miR-3679-3p,miR-642a-5p		
26	25358669	T	C	Novel 7					GGTAATTTAGATGAATTTAGGGGaaAAAAaAGTTATCTGCAGAtATGTT	miR-5195-5p,miR-3158-5p,miR-135a-5p,miR-4775	miR-5195-5p,miR-3158-5p,miR-135a-5p,miR-4776, miR-629-3p	miR-629-3p		
27	25358664	T	C	Novel 8					TTTAGATGAATTTAGGGGaaAAAAaAGTTATCTGCAGAtATGTTGAGGG	miR-1277-5p,miR-3158-5p,miR-135a-5p,miR-4775	miR-3158-5p		miR-1277-5p,miR-135a-5p,miR-4775	
28	25358650	A	T	rs12245	none	none	miR-544		GGGaaAAAAaAGTTATCTGCAGAtATGTTGAGGGCCCATCTCTCCC	miR-1277-5p,miR-654-5p,miR-4644	miR-654-5p,miR-4644,miR-3143,miR-16-2-3p,miR-544a	miR-3143, miR-16-2-3p, miR-544a	miR-1277-5p	
29	25358418	T	C	rs61764374					AACTGAAACATGCACATTTTGTACaTTGTGCTTTCTTTTGTGGGACATA	miR-3171,miR-4311,miR-3613-3p,miR-548x-5p,miR-548aj-5p,miR-524-5p,miR-1283,miR-548g-5p	miR-330-3p,miR-4311,miR-3613-3p,miR-548x-5p,miR-548aj-5p,miR-524-5p,miR-1283,	miR-330-3p, miR-3678-5p	miR-3171	

											miR-3678-5p, miR-548g-5p			

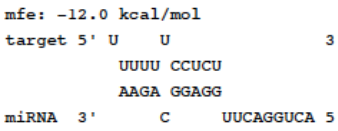
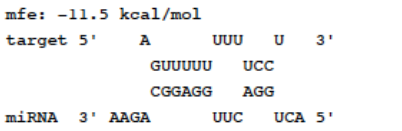
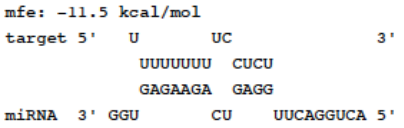
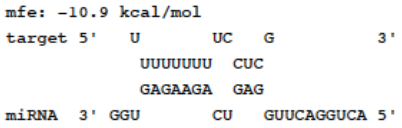
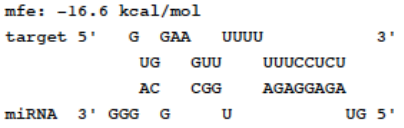
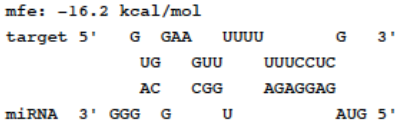
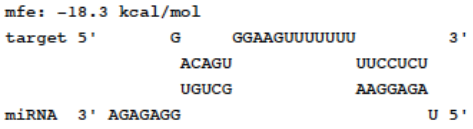
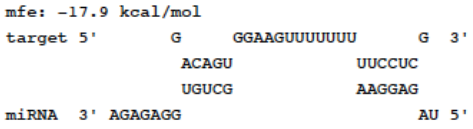
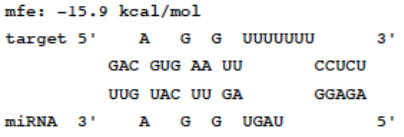
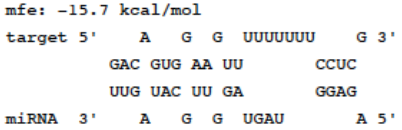
Sup. Table 7. The effects of the variants identified in EOC cases on putative miRNA complementary sites

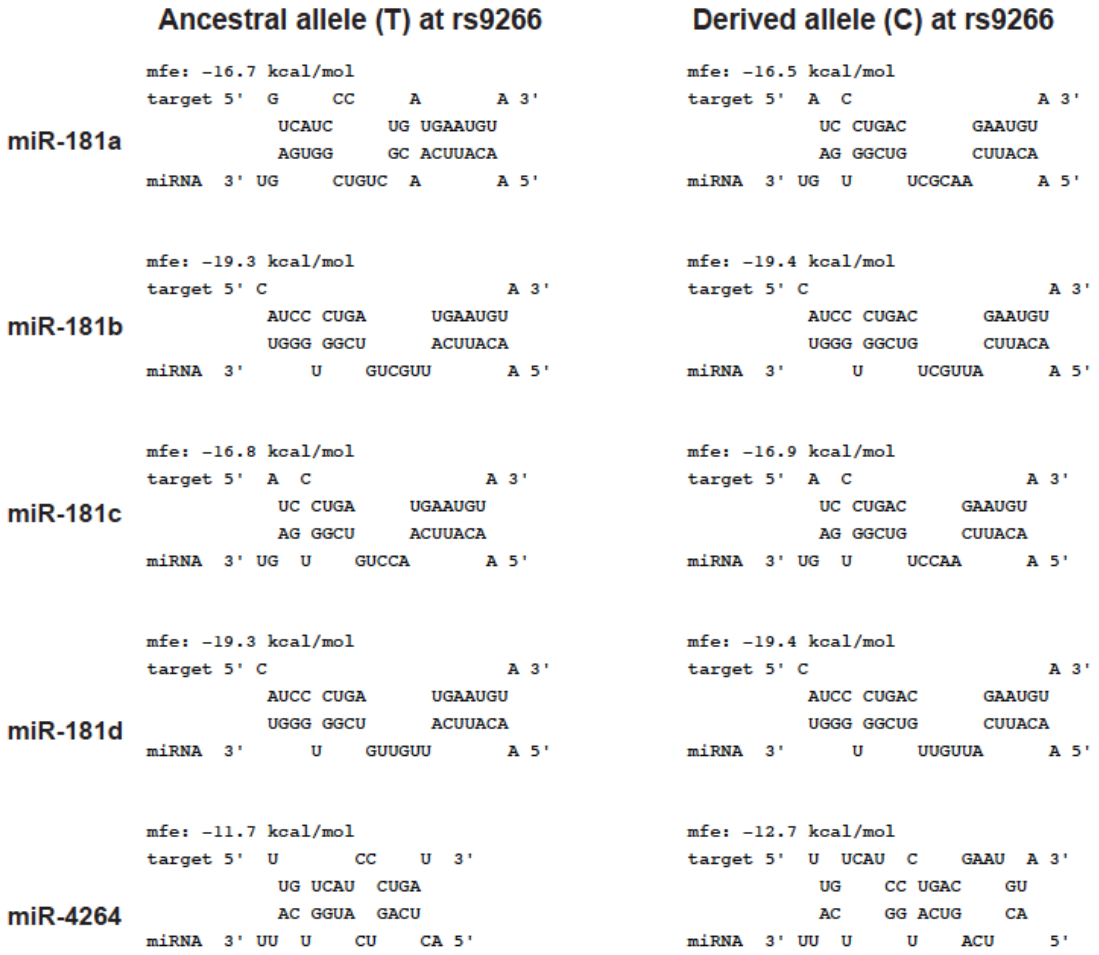
Patrocles with a 8-mer setting, and miRNASNP with a default setting were utilized. Target sequences including alternative alleles were used to predict gain or loss of miRNA complementary sites by the derived allele using the miRanda algorithm with a default setting.



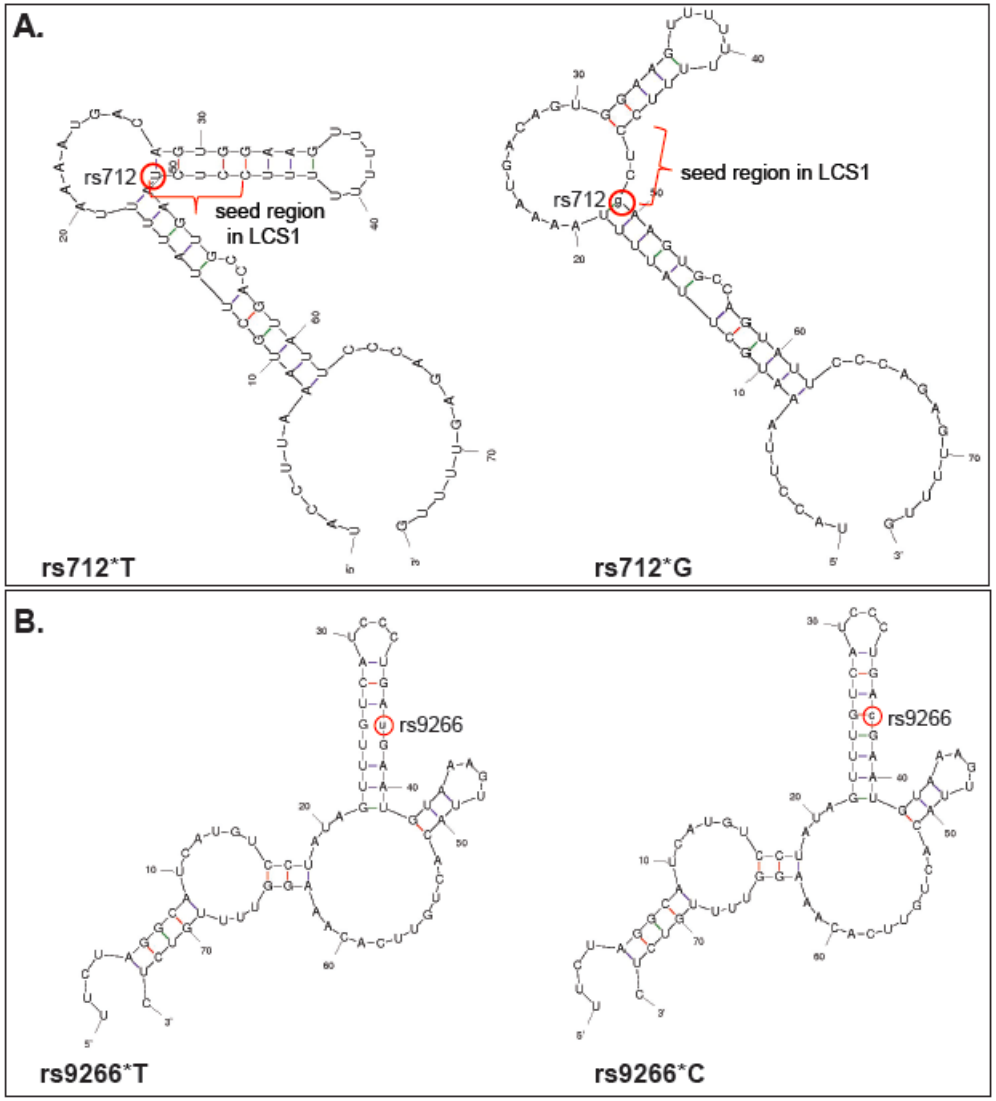
Sup. Figure 1. The haplotypes with rs712, rs9266, rs61764370 and additional 10 tagging SNPs

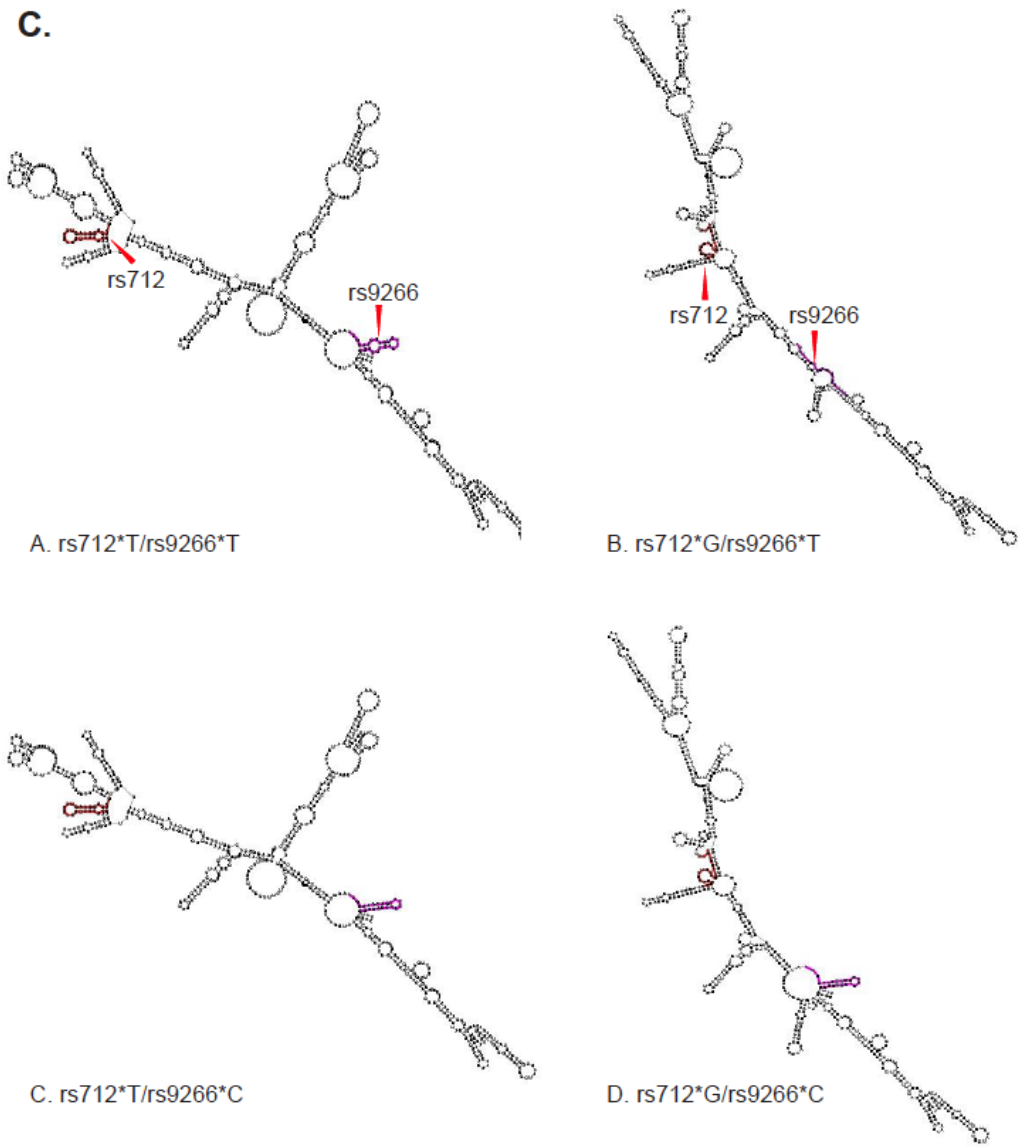
These 11 SNPs include five SNPs in an adjacent intron (rs17329025, rs17388148, rs12424283, rs10842508, and rs4963859), one SNP in the *KRAS* transcript variant A (rs1137282), four SNPs in the 3' UTR of the *KRAS* transcript variant B (rs9266, rs7973450, rs13096, and rs12587) and one SNP in an intergenic region of the 3' UTR of the *KRAS* (rs11047892). In all eight haplotypes that were identified, the derived alleles (the G alleles) at rs712 and rs61764370 were never found together in cis.

	Ancestral allele (T) at rs712	Derived allele (G) at rs712
miR-378b		
miR-378c		
miR-877		
miR-3125		
let-7d		

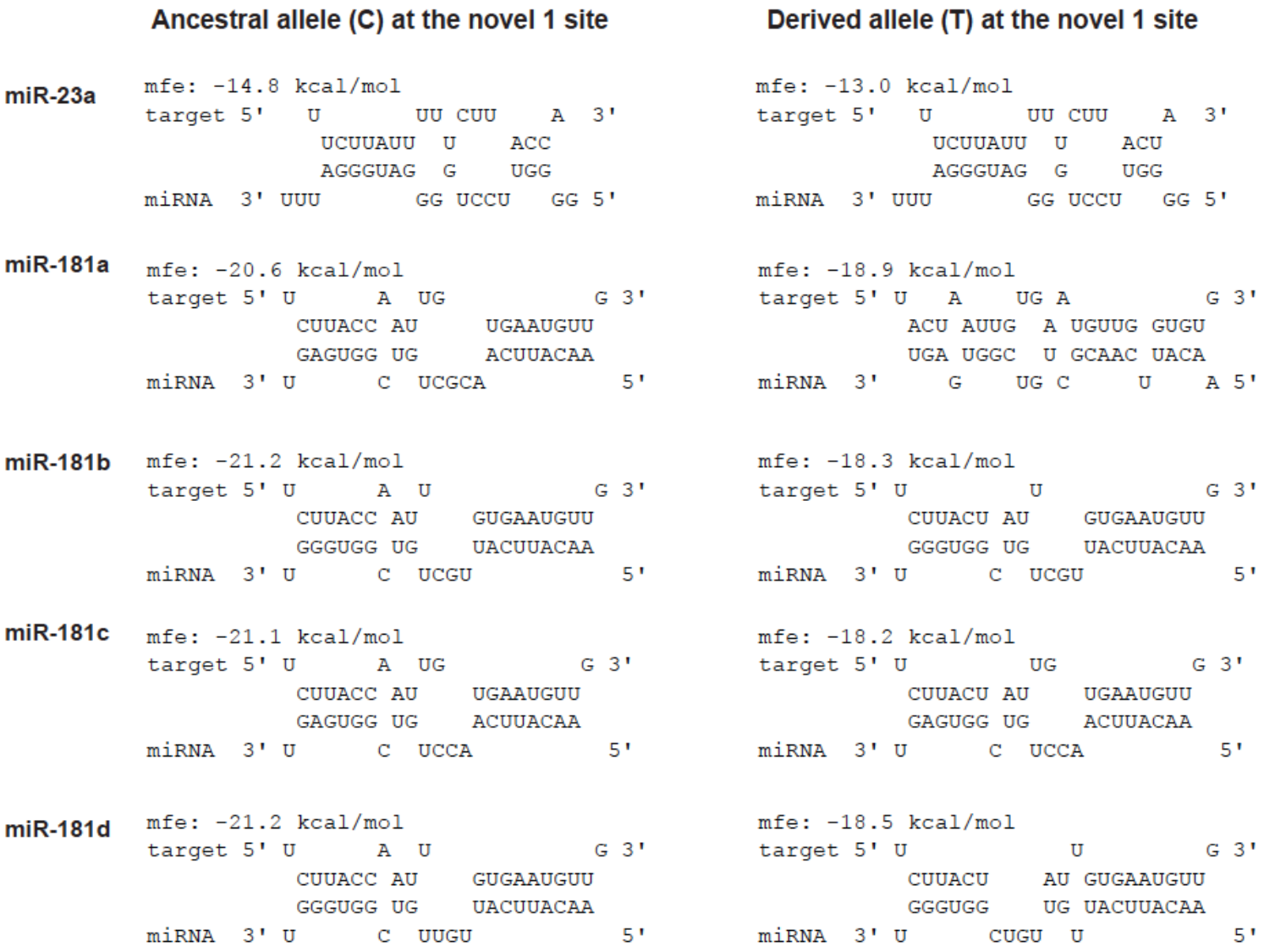


Sup. Figure 2. The effect of the derived alleles at rs712 and rs9266 on the *KRAS* mRNA/miRNA duplexes
Minimum free energies required to form a duplex between an individual miRNA and predicted high confidence miRNA complementary site with the derived or ancestral allele at rs712 and rs9266 (RNAhybrid).


A.
rs712
seed region
in LCS1
rs712*T
rs712
seed region in LCS1
rs712*G
B.
rs9266
rs9266*T
rs9266
rs9266*C



Sup. Figure 3. The effect of the derived alleles at rs712 and rs9266 on the RNA secondary structures
A. The effect of the derived allele at rs712 on the secondary structure of the selected region near LCS1 (Mfold)
B. The effect of the derived allele at rs9266 on the secondary structure of the selected region (Mfold)
C. The effects of the derived alleles at rs712 and rs9266 on the secondary structure of the exact length of a fragment in the reporter constructs. (The UEA sRNA toolkit) Red: LCS1 with rs712. Pink: miR-181 complementary site with rs9266. Arrow indicates the SNP site.



Sup. Figure 4. The effect of the novel variant (novel 1) on the *KRAS* mRNA/miRNA duplexes
Minimum free energies required to form a duplex between an individual miRNA and predicted high confidence miRNA complementary site with the derived or ancestral allele at the novel varying site (RNAhybrid).

SMJ104	CTAGCTAGCATACAATTTGTACTTTTTTCTTAAGGCATAC
LJC1	GGCACACCACCACCCCAAAATCTC
LJC2	CCATCTTCAGTGCCAGTCTTGGG
LJC3	GGGTCGTATACCAAAGGCCTTAG
LJC4	GCCTGAACTAGTTCACAGACAAGGG
LJC5	CTAGCTAGCTCAATGCAGAATTCATGCTATCCAG
MK5	TGCTTTTGTTTCTTAAGAAAACAAACTC
MK6	GAAGAGTCCTAAAACGAGAATGGATATTC
MK7	TACCAGATGCCAGTCACCGCAC
MK8	CTGAAGTATGGCCATTTCTTTCTCTG
MK10	GTGTAGTAATGTTTTTTAGAACCCAGCAG
MK11	TTCCTAGGTCAGCGCAACCAAATG
MK12	GTGTAAACTGAAACATGCACATTTTGTAC
MK13	GGTTCACTACAAAACAAACAGTTCCTG

Sup. Table 8. Primers used to amplify and sequence the *KRAS* 3′ UTR in NSCLC cases