

Figure S1: GO and KEGG analysis of the target genes of hsa-miR-221.

Notes: GO enrichment of target genes in (A) biological process ontology, (B) molecular function ontology and (C) cellular component ontology. (D) Significantly enriched pathway terms of the target genes.

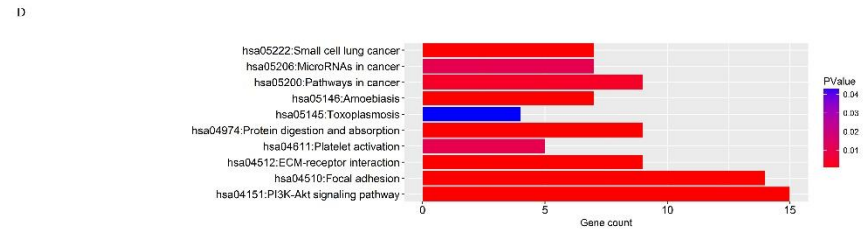
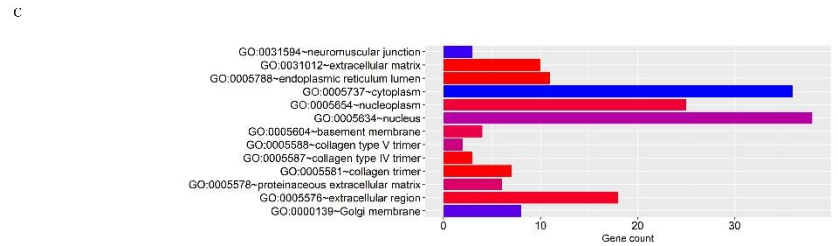
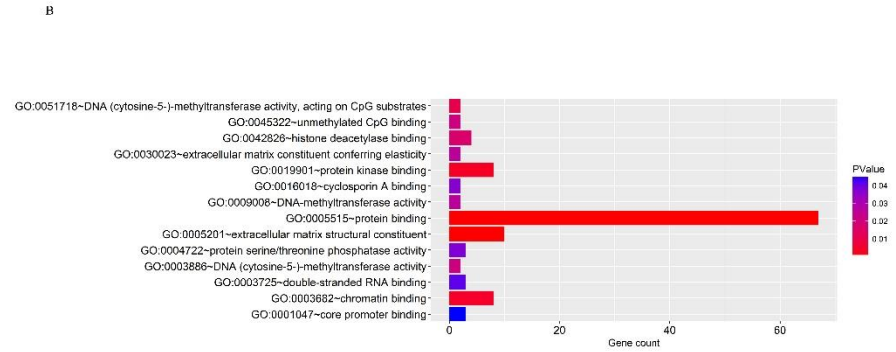
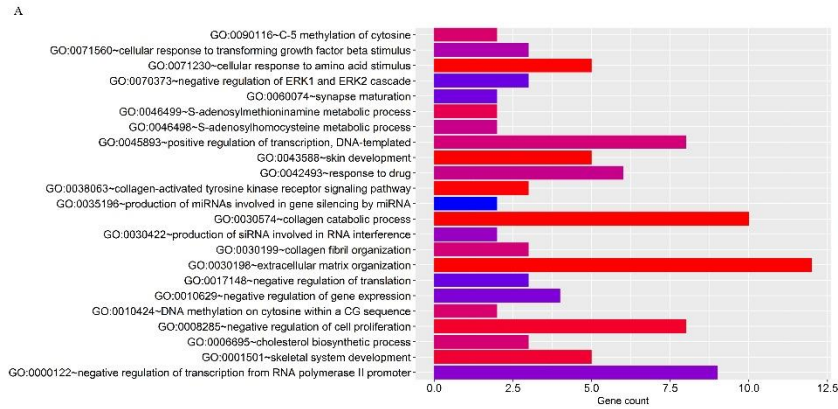


Figure S2: GO and KEGG analysis of the target genes of hsa-miR-29c.

Notes: GO enrichment of target genes in (A) biological process ontology, (B) molecular function ontology and (C) cellular component ontology. (D) Significantly enriched pathway terms of the target genes.

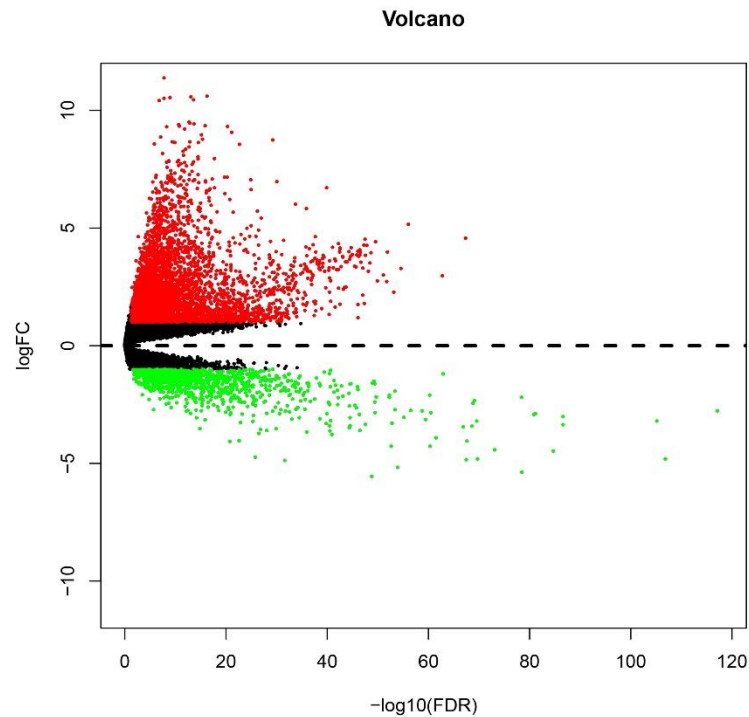


Figure S3: Volcano plot of the aberrantly expressed mRNAs between HCC tissues and normal liver tissues.

Notes: Red dots indicate high expression and green dots indicate low expression of miRNAs. Black dots show the miRNAs with expression of $|\log_2FC| < 1$. The X axis represents an adjusted FDR value and the Y axis represents the value of \log_2FC . Aberrantly expressed miRNAs were calculated by edgeR R. Altogether, 3847 high and 1048 low expressed miRNAs were achieved. This volcano plot was conducted by the ggplot2 package of R language.

miRNA combination vs the 7-miRNA classifier

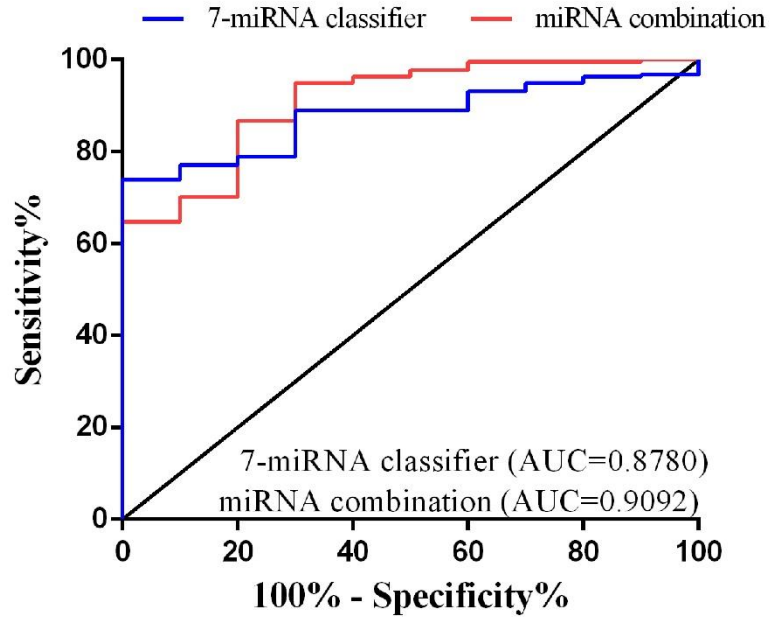


Figure S4: ROC curves to compare the diagnostic accuracy between the miRNA combination and the 7-miRNA classifier of *Lin et al.*

Notes: The X axis shows false positive rate, presented as “100%-Specificity%”. The Y axis indicates true positive rate, shown as “Sensitivity%”.

These curves were provided by GraphPad Prism 6.

Table S1 Information of 5 datasets used in this study

Dataset	Platform	Experiment type	Number of genes in original study	Number of genes used in this study	Expression type
GSE12717	GPL7274	Non-coding RNA profiling by array	347	313	log2-transformed
GSE10694	GPL6542	Non-coding RNA profiling by array	121	110	log2-transformed
GSE74618	GPL14613	Non-coding RNA profiling by array	13854	2	log2-transformed
TCGA-LIHC(miRNA)	NA	High throughput sequencing	1881	2	BCGSC
TCGA-LIHC(mRNA)	NA	High throughput sequencing	17793	4895	HTSeq-Counts

Table S2 Significantly differentially expressed miRNAs of screening datasets GSE12717

miRNA	Log FC	P Value
hsa-miR-222	2.491835	0.000312
hsa-miR-378	-2.5645	0.000379
hsa-miR-422a	-2.61368	0.001059
hsa-miR-25	1.949887	0.001366
hsa-miR-362	1.790857	0.001448
hsa-miR-301	2.156216	0.001594
hsa-miR-18b	1.898096	0.001611
hsa-miR-520a	-2.31525	0.001677
hsa-miR-93	2.217326	0.003224
hsa-miR-221	1.887786	0.004491
hsa-miR-424	-3.49307	0.005137
hsa-miR-491	2.380884	0.005531
hsa-miR-139	-2.43037	0.006522
hsa-miR-18a	1.550395	0.006919
hsa-miR-184	-2.6436	0.007052
hsa-miR-195	-2.16606	0.007289
hsa-miR-106b	1.929812	0.007399
hsa-miR-499	-1.79363	0.008043
hsa-miR-126*	-2.57251	0.008434
hsa-miR-223	-1.96291	0.009474
hsa-miR-224	4.666059	0.009586
hsa-miR-299-5p	1.52338	0.011292

hsa-miR-335	-1.70856	0.012899
hsa-miR-497	-1.8116	0.013861
hsa-miR-520f	-3.36844	0.013892
hsa-miR-9	1.72739	0.016631
hsa-miR-133a	-1.82079	0.016835
hsa-miR-105	-1.03203	0.019724
hsa-miR-210	1.827347	0.021065
hsa-miR-422b	-3.51606	0.022023
hsa-miR-452	3.842516	0.024444
hsa-miR-450	-1.30479	0.025978
hsa-miR-29c	-2.27737	0.03304
hsa-miR-346	-1.13176	0.033247
hsa-miR-100	-1.8959	0.033891
hsa-miR-203	-1.75096	0.035834
hsa-miR-370	1.481095	0.036387
hsa-miR-452*	2.621289	0.037074
hsa-miR-520c	-2.53422	0.038798
hsa-miR-125b	-2.3884	0.038951
hsa-miR-189	-1.26582	0.041251
hsa-miR-106a	1.189188	0.041355
hsa-miR-302a	-1.28387	0.041961
hsa-miR-101	-1.82946	0.041984
hsa-let-7e	-1.65266	0.042728
hsa-miR-199a	-2.36837	0.045643
hsa-miR-217	2.646149	0.046473

hsa-miR-340	-1.73691	0.04666
hsa-miR-17-5p	1.080435	0.047621
hsa-miR-216	2.267764	0.04939

Abbreviations: FC: fold change

Table S3 Significantly differentially expressed miRNAs of training dataset GSE10694

miRNA	Log FC	adj.P value
hsa-miR-221	2.665307	5.11E-11
hsa-miR-520f	-1.19342	8.42E-10
hsa-miR-520d	-1.15423	8.42E-10
hsa-miR-422a	-1.03471	1.36E-09
hsa-miR-222	2.385102	1.36E-09
hsa-miR-101	-2.10304	3.77E-09
hsa-miR-29c	-1.84006	2.17E-08
hsa-miR-25	1.690017	2.23E-07
hsa-miR-424	-1.63196	3.03E-07
hsa-miR-34a	1.468384	3.18E-07
hsa-miR-188	-1.52903	3.57E-07
hsa-miR-191	1.637212	6.91E-07
hsa-miR-15b	1.763118	7.69E-07
hsa-let-7i	1.058211	7.98E-07
hsa-miR-103	1.115363	2.54E-06
hsa-miR-148a	-1.29407	3.40E-06
hsa-miR-30d	1.166132	1.85E-05
hsa-miR-26b	-1.1027	0.000132
hsa-miR-93	1.128434	0.000155
hsa-miR-215	-1.4757	0.000156
hsa-miR-181a	1.321599	0.000199
hsa-miR-29b	-1.06747	0.000242

hsa-miR-106b	1.270324	0.000267
hsa-miR-342	1.24591	0.000343
hsa-miR-451	-1.47535	0.00046
hsa-miR-150	1.115177	0.003204
hsa-miR-202	-1.00898	0.023244

Abbreviations: FC: fold change

Table S4 Target genes of hsa-miR-221 and hsa-miR-29c

miRNA	Target gene
hsa-miR-221	ARF4 ^[1] , ARID1A ^[2] , ARNT ^[3] , CBFβ, CDKN1B ^[4] , CTCF ^[5] , EIF5A2, ESR1 ^[6] , FOS ^[7] , GNAI2, HECTD2, HIPK1, INSIG1, MYLIP, MYO10, NLK ^[8] , PAIP2, POGZ, PPP6C, RAB1A ^[9] , TCF12, TIMP3 ^[10] , TRPS1 ^[11] , UBE2J1, VAPB, VGLL4, YWHAG,
hsa-miR-29c	ABCB6, AKT3, AMOT, AP1G1, ARRDC3, ATP5G1, BLMH, BMF, C5orf15, CAV2, CCND2 ^[12] , CCNT2, CDC42 ^[13] , CHIC2, CHSY1, COL15A1, COL19A1, COL3A1 ^[14, 15] , COL4A1 ^[16] , COL4A2, COL4A5 ^[17] , COL5A2, COL5A3, COL6A3, COL7A1, COMMD2, CPEB3, DICER1, DNMT3A ^[14] , DNMT3B ^[18] , EIF4E2, ELF2, ELOVL4, FBN1 ^[15] , FEM1B, FOXJ2, GNG12, GPX7, HBP1, HDAC4 ^[19] , HMGCR, HMGCS1, IFI30, INSIG1, IREB2, ITGB1 ^[20] , KCTD5, KLF4, KLHDC3, LAMC1, LDOC1L, MCL1 ^[21] , MFAP3, MORF4L1, MYCN, NAV1, NAV3 ^[22] , NFIA, NKTR, PARG, PCDHA9, PDHX, PLXNA1, PMP22, PPIC ^[23] , PPM1D, PPP1R13B, PPP1R15B, PRKRA, PTEN ^[24] , RAB30, REV3L ^[25] , RLF, RNF138, RNF39, SESTD1, SFPQ, SLC16A1, SLC31A1, SOX12, SPRY1, SS18L1, SUV420H1, SUV420H2, TAF5, TDG, TNFRSF1A, TP53INP1, USP37, WDFY1, ZBTB5, ZDHHC5, ZFP36L1, ZFP91, ZNF282, ZNF346,

Table S5 Hub target genes of hsa-miR-221 and hsa-miR-29c

miRNA	Hub target gene
hsa-miR-221	ESR1, FOS
hsa-miR-29c	COL15A1, COL4A1, COL4A2, COL4A5, COL5A3, COL7A1, DNMT3A, DNMT3B, ELOVL4, HDAC4, LAMC1, MYCN, NAV3, PCDHA9, PLXNA1, SOX12,

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