Supplementary materials:

Table S1: Primer sequences for HallMark-32

microRNA target	Primer Sequence
miR-101-3p	CGCATACAGTACTGTGATAACTGAA
miR-122-5p	TGG AGT GTG ACA ATG GTG TTT G
miR-1246	GCAATGGATTTTTGGAGCA
miR-125A-5P	GAGACCCTTTAACCTGTGAAAAA
miR-125b-5p	CTC CCT GAG ACC CTA ACT TGT G
miR-145-5p	CAGTTTTCCCAGGAATCCCTAA
miR-148a-3p	CGC TCA GTG CAC TAC AGA ACT TT
miR-150-5p	TCCCAACCCTTGTACCAGTGAA
miR-18a-5p	AAGGTGCATCTAGTGCAGATAGAAA
miR-191-5p	AAC GGA ATC CCA AAA GCA G
miR-192-5p	CTG ACC TAT GAA TTG ACA GCC AAA
miR-193a-5p	GTC TTT GCG GGC GAG AT
miR-19a-3p	TGTGCAAATCTATGCAAAACTGA
miR-21-5p	AGC TTA TCA GAC TGA TGT TGA AAA A
miR-214-3p	GCA CAG CAG GCA CAG ACA G
miR-22-5p	AGT TCT TCA GTG GCA AGC TTT A
miR-221-3p	GCG AGC TAC ATT GTC TGC TG

miR-222-3p	GCT ACA TCT GGC TAC TGG GTA AA
miR-223-3p	TGT CAG TTT GTC AAA TAC CCC AAA
miR-23a-3p	ACA TTG CCA GGG ATT TCC AA
miR-26a-5p	TTC AAG TAA TCC AGG ATA GGC TAA A
miR-29a-3p	GCA CCA TCT GAA ATC GGT TAA A
miR-30c-5p	GCA GCA TGT AAA CAT CCT ACA CTC T
miR-320d	AAAGCTGGGTTGAGAGGAAA
miR-365a-3p	CGTAATGCCCCTAAAAATCCTT
miR-374a-5p	CGCCTTATAATACAACCTGATAAGTG
miR-423-3p	TGAGGCCCCTCAGTAAAAA
miR-423-5p	GGGCAGAGAGCGAGACTTTA
miR-424-5p	GCAGCAATTCATGTTTTGAA
miR-451a	CGA AAA CCG TTA CCA TTA CTG A
miR-486-5p	GAGCTGCCCCGAGAAAAA
miR-574-3p	CTCATGCACACACCCACAA

Table S2: The reported evidence of HallMark-32 microRNAs in regulating cancer hallmarks

miRNA	Sustaining Proliferative Signaling	Evading Growth Suppressors	Avoiding Immune Destruction	Enabling Replicative Immortality	Tumor Promoting Inflammation	Activating Invasion / Metastasis	Inducing Angiogenesis	Genome Instability	Resisting Cell Death	Deregulating Cellular Energetics
150-5p	[2]					[1]				
574-3p		[52]								
125b-5p	[3]	[4]				[3]			[4]	
191-5p						[5]				
101-3p	[7]					[7]			[6]	[8]
1246	[9]			[48]		[10]			[9]	
21-5p	[11]			[49]		[11]				
23a-3p		[13]	[12]							
145-5p	[14]	[15]				[14]			[16]	
125a-5p						[18]			[17]	
214-3p	[19]	[20]				[19]				
192-5p				[50]					[21]	
320d	[22]									
18a-5p	[23]								[23]	
26a-5p	[24]					[24]			[24]	
193a-5p	[25]								[25]	
365a-3p										
19a-3p	[28]					[27]				
148a-3p				[51]	[29]	[30]	[30]			
222-3p	[31]								[31]	
423-3p		[32]					[33]			
486-5p	[34]					[34]				
22-5p										[53]
223-3p	[35]								[35]	
423-5p		[32]	[36]						[37]	
374a-5p	[38]					[38]		[38]		
221-3p						[40]		[39]		
30c-5p					[54]					
424-5p	[41]	[42]	[44]			[41]	[43]			
122-5p	[45]					[45]				
29a-3p	[46]					[46]				
451a	[47]					[47]				

Table S3: Expression level of miRNAs in HallMark-32 and the *p*-values results in t-test and ANOVA analysis. Notes: * *p*-values ≤ 0.05; ** *p*-values ≤ 0.01; High CTC value means low microRNA expression.

miRNA	**Mean**			**SEM**			**Fold-change relative to Healthy**			**HCC vs. CRCLM (p-value)**	**HCC vs. Healthy (p-value)**	**HCC vs. CRCLM vs. Healthy (p-value)**
	HCC	**Healthy**	**CRCLM**	**HCC**	**Healthy**	**CRCLM**	**HCC**	**Healthy**	**CRCLM**			
101-3p	24.25	24.37	23.6	0.24	1.04	0.26	1.09	1	1.71	0.069	0.909	0.319
122-5p	28.75	29.12	28.84	0.26	0.64	0.23	1.29	1	1.21	0.796	0.593	0.783
1246	25.41	25.73	24.01	0.2	0.95	0.31	1.25	1	3.28	0.000**	0.744	0.005**
125a-5p	30.01	30.37	30.1	0.22	0.24	0.16	1.28	1	1.2	0.725	0.277	0.587
125b-5p	31.38	30.73	30.77	0.21	0.46	0.28	0.64	1	0.98	0.082	0.207	0.218
145-5p	32.34	31.32	30.19	0.27	0.69	0.33	0.49	1	2.18	0.000**	0.170	0.000**
148a-3p	27.59	27.1	26.33	0.23	0.59	0.22	0.71	1	1.71	0.000**	0.443	0.003**
150-5p	28.77	27.62	27.66	0.28	0.85	0.26	0.45	1	0.97	0.004**	0.202	0.041*
18a-5p	27.66	27.39	26.9	0.25	0.63	0.24	0.83	1	1.41	0.028*	0.688	0.146
191-5p	27.74	27.05	26.1	0.24	0.9	0.22	0.62	1	1.94	0.000**	0.463	0.001**
192-5p	29.64	29.34	29.15	0.19	0.46	0.18	0.81	1	1.13	0.062	0.541	0.252
193a-5p	33.25	33.24	32.66	0.16	0.37	0.31	0.99	1	1.5	0.093	0.971	0.228
19a-3p	23.42	23.58	22.43	0.25	1.07	0.24	1.12	1	2.21	0.005**	0.884	0.079
21-5p	24.43	24.24	23.19	0.19	0.52	0.21	0.87	1	2.06	0.000**	0.721	0.000**
214-3p	28.58	29.67	28.72	0.18	0.75	0.13	2.13	1	1.94	0.550	0.164	0.047*
22-5p	30.59	30.1	29.36	0.21	0.46	0.21	0.71	1	1.68	0.000**	0.339	0.001**
221-3p	28.15	27.27	26.29	0.21	0.36	0.25	0.55	1	1.97	**0.000****	**0.042***	**0.000****
222-3p	29.65	29.43	28.47	0.21	0.79	0.22	0.86	1	1.95	0.000**	0.788	0.01**
223-3p	25.72	24.14	22.81	0.25	0.73	0.28	0.33	1	2.51	**0.000****	**0.045***	**0.000****
23a-3p	28.04	26.94	25.69	0.21	0.57	0.24	0.47	1	2.38	0.000**	0.077	0.000**
26a-5p	28.14	26.77	26.1	0.26	0.62	0.25	0.39	1	1.6	**0.000****	**0.046***	**0.000****
29a-3p	26.54	26.27	25.19	0.23	0.93	0.24	0.83	1	2.12	0.000**	0.781	0.011**
30c-5p	25.85	25.04	25.05	0.17	0.31	0.17	0.57	1	0.99	**0.001****	**0.026***	**0.004****
320d	33.44	33.61	32.64	0.22	0.31	0.21	1.13	1	1.96	0.01**	0.657	0.009**
365a-3p	28.63	29.2	28.75	0.12	0.2	0.09	1.48	1	1.37	**0.474**	**0.018****	**0.027***
374a-5p	28.38	27.51	27	0.29	0.67	0.23	0.55	1	1.43	0.000**	0.240	0.005**
423-3p	29.51	30.35	29.54	0.23	0.23	0.19	1.79	1	1.75	**0.917**	**0.012****	**0.062**
423-5p	28.69	28.34	27.69	0.2	0.52	0.25	0.79	1	1.57	0.002**	0.542	0.02*
424-5p	28.03	27.85	26.64	0.21	0.87	0.24	0.88	1	2.31	0.000**	0.840	0.004**
451a	17.8	17.91	17.33	0.25	1.01	0.22	1.09	1	1.5	0.161	0.910	0.496
486-5p	24.41	24.17	24.08	0.17	0.42	0.16	0.85	1	1.06	0.168	0.598	0.469

574-3p	31.37	31.09	30.6	0.14	0.26	0.17	0.82	1	1.4	0.001**	0.346	0.004**

Table S4: Data overview for the sample quality data in HCC, Healthy, and CRCLM

Samples quality data	Median			SEM		
	HCC	Healthy	CRCLM	HCC	Healthy	CRCLM
miR-150-5p specificity	1.00	1.00	1.00	0.00	0.05	0.00
miR-547-3p specificity	0.50	1.00	0.50	0.93	0.06	0.04
miR-125b-5p specificity	1.00	1.00	1.00	0.00	0.03	0.02
miR-191-5p specificity	1.00	1.00	1.00	0.00	0.00	0.01
miR-101-3p specificity	1.00	1.00	1.00	0.00	0.05	0.00
miR-1246 specificity	1.00	1.00	1.00	0.00	0.05	0.01
miR-21-5p specificity	1.00	1.00	1.00	0.00	0.05	0.00
miR-23a-3p specificity	1.00	1.00	1.00	0.03	0.05	0.01
miR-145-5p specificity	1.00	1.00	1.00	0.00	0.05	0.00
miR-125a-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-214-3p specificity	0.25	0.75	0.25	0.05	0.08	0.05
miR-192-5p specificity	1.00	1.00	1.00	0.03	0.06	0.00
miR-320d specificity	1.00	1.00	1.00	0.02	0.00	0.00
miR-18a-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-26a-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-193a-5p specificity	0.50	1.00	1.00	0.05	0.08	0.04
miR-365a-3p specificity	1.00	0.50	0.50	0.02	0.05	0.03
miR-19a-3p specificity	1.00	1.00	1.00	0.00	0.05	0.00
miR-148a-3p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-222-3p specificity	1.00	1.00	1.00	0.00	0.05	0.02
miR-423-3p specificity	1.00	1.00	1.00	0.02	0.00	0.02
miR-486-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-22-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-223-3p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-423-5p specificity	1.00	1.00	1.00	0.00	0.00	0.01
miR-374a-5p specificity	1.00	1.00	1.00	0.00	0.00	0.00
miR-221-3p specificity	1.00	1.00	1.00	0.05	0.00	0.04

miR-30c-5p specificity	1.00	1.00	1.00	0.03	0.04	0.02
miR-424-5p specificity	1.00	1.00	1.00	0.00	0.02	0.00
miR-122-5p specificity	1.00	1.00	1.00	0.02	0.03	0.00
miR-29a-3p specificity	1.00	1.00	1.00	0.00	0.02	0.00
miR-451a specificity	1.00	1.00	1.00	0.00	0.00	0.01
RNA amount (ug/uL)	23.00	47.00	51.50	5.57	13.19	8.34
A260/A280 from RNA	1.19	1.27	1.12	0.03	0.07	0.03
A260/A230 from RNA	0.06	0.09	0.09	0.02	0.04	0.01
DNA amount (ug/uL)	1430.55	1533.50	1565.70	24.23	32.10	19.50
A260/A280 from cDNA	2.11	2.16	2.13	0.02	0.01	0.01
A260/A230 from cDNA	1.79	1.78	1.62	0.04	0.07	0.03

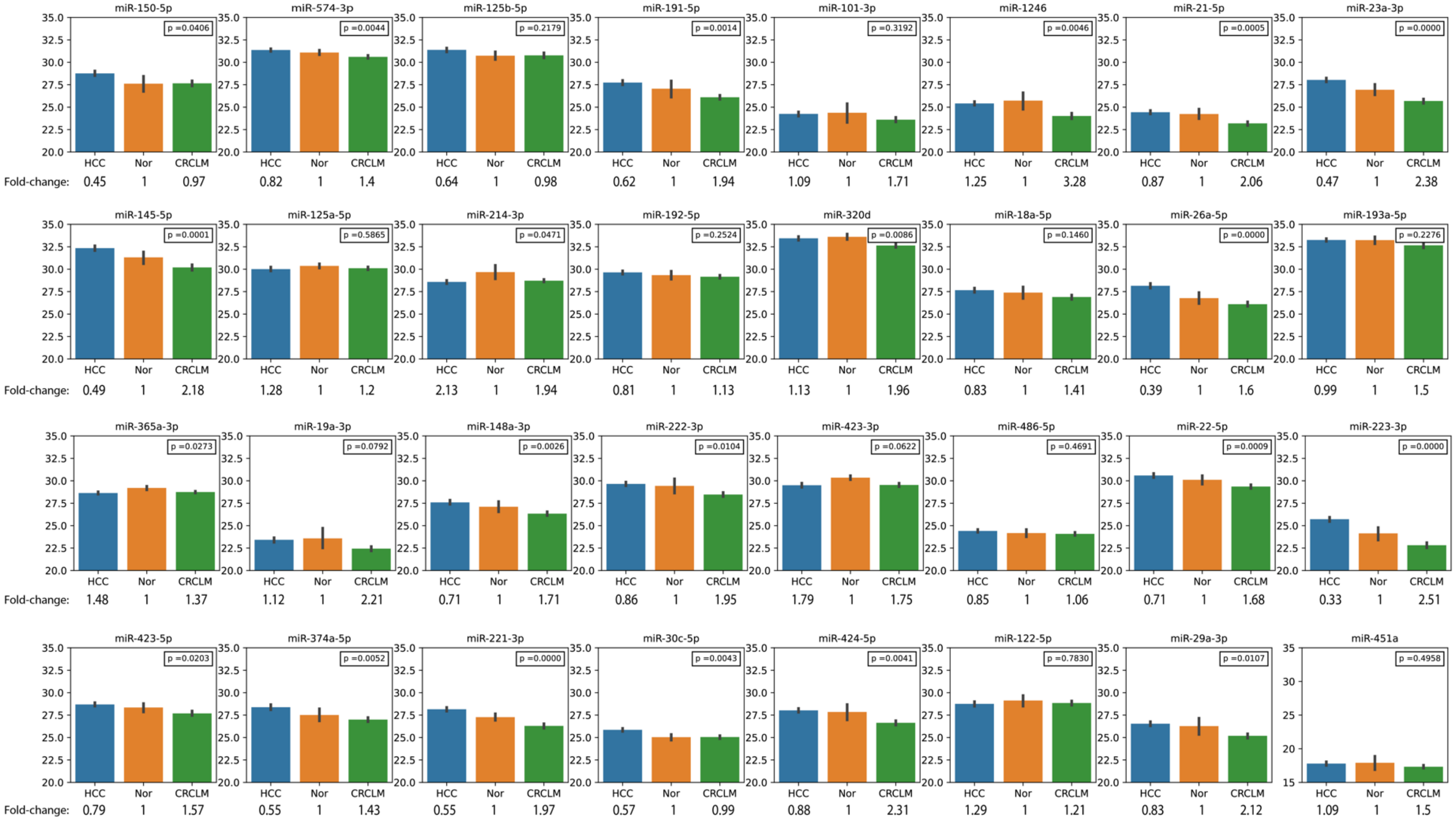
Table S5: Ten cancer hallmarks in HCC and their associated molecular pathways [55]

HCC Hallmarks	Molecular Mechanism of HCC induced by HBV
Sustaining Proliferative Signaling	PI3K/Akt, Ras/Raf/MAPK, Src, YAP, Wnt/β-catenin, cyclin D, c-myc, c-jun, EGFR, ccND1, TGF-β, Clusterin, DNMT3b, NOX-4, STAT3
Evading growth suppressors	p53, p18
Avoiding immune destruction	Immune dysregulation, IFN-β, PDL-1, TGF-β, IL-28
Enabling replicative immortality	HBV DNA integration, nTERT
Tumor promoting inflammation	Endoplasmic reticulum ROS, NF-Kβ, TNF-α, GSTP1, Mitochondria ROS, IL-6
Activating invasion and metastasis	TGF-β, IncRNA-ATB
Inducing angiogenesis	VEGF, HIFα, MTA1
Genome instability and mutation	Endoplasmic reticulum ROS, HBV DNA integration, Mitochondria ROS, UV-DDBI
Resisting cell death	p53, p18 mcl-1, Notch, apoptosis, HBV DNA integration
Deregulating cellular energetics	Hypoxia induced lactic acid biosynthesis

Table S6: Probability cut-off values and the associated sensitivity and specificity in ROC curve analysis

	HallMark-32 sample quality-adjusted model (n=133)	
Probability Cut-off	**Sensitivity**	**1 - Specificity**
0.29	1.00	0.05
0.39	1.00	0.04
0.55	1.00	0.02
0.61	0.98	0.02
0.63	0.98	0.01
0.66	0.96	0.01
0.72	0.94	0.01
0.78	0.92	0.01

Figure S1: Bar chart of 32 miRNA CT values in HCC, Healthy and CRCLM groups and fold change relative to healthy. The *p*-values at the top right corner represent the *p*-values in the ANOVA test comparing the CT values in three groups (HCC, Healthy and CRCLM).



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