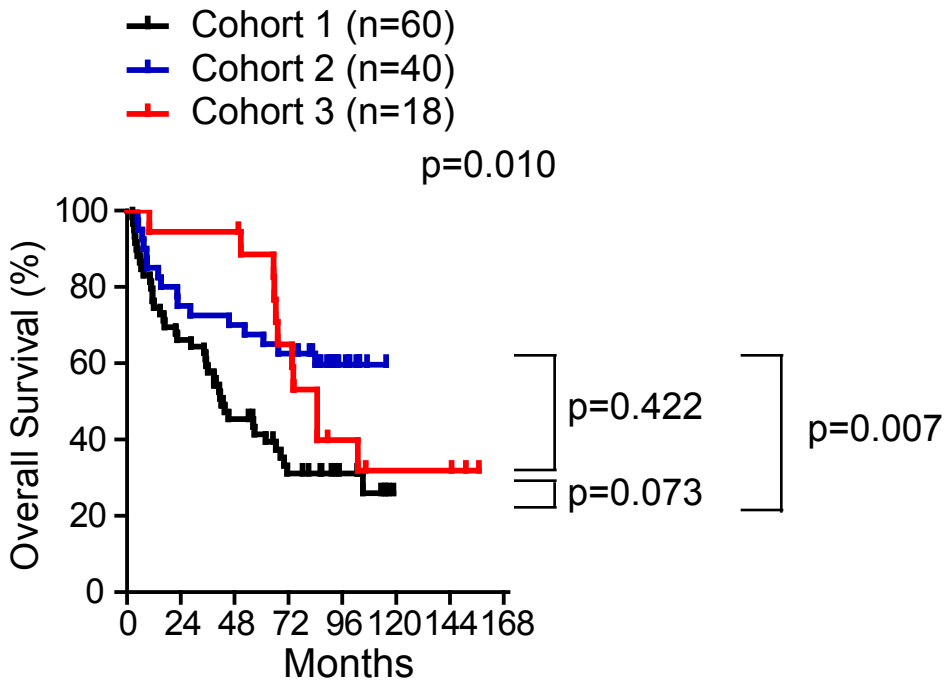
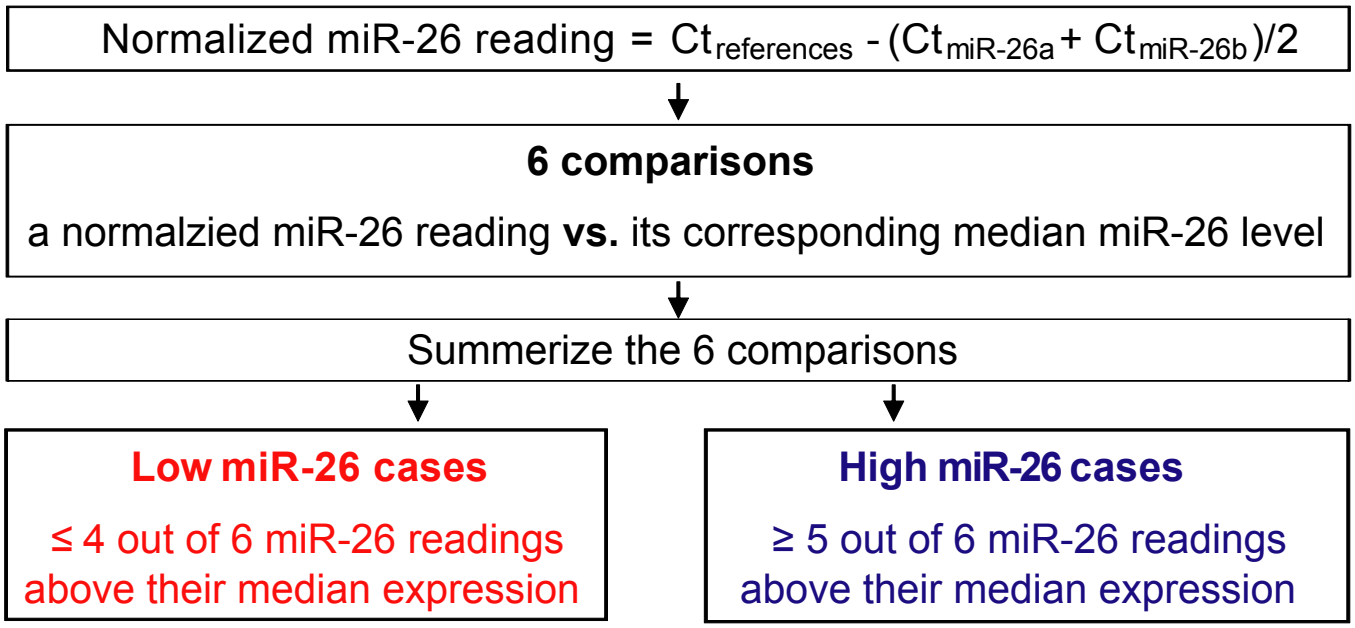
Supplementary Fig 1

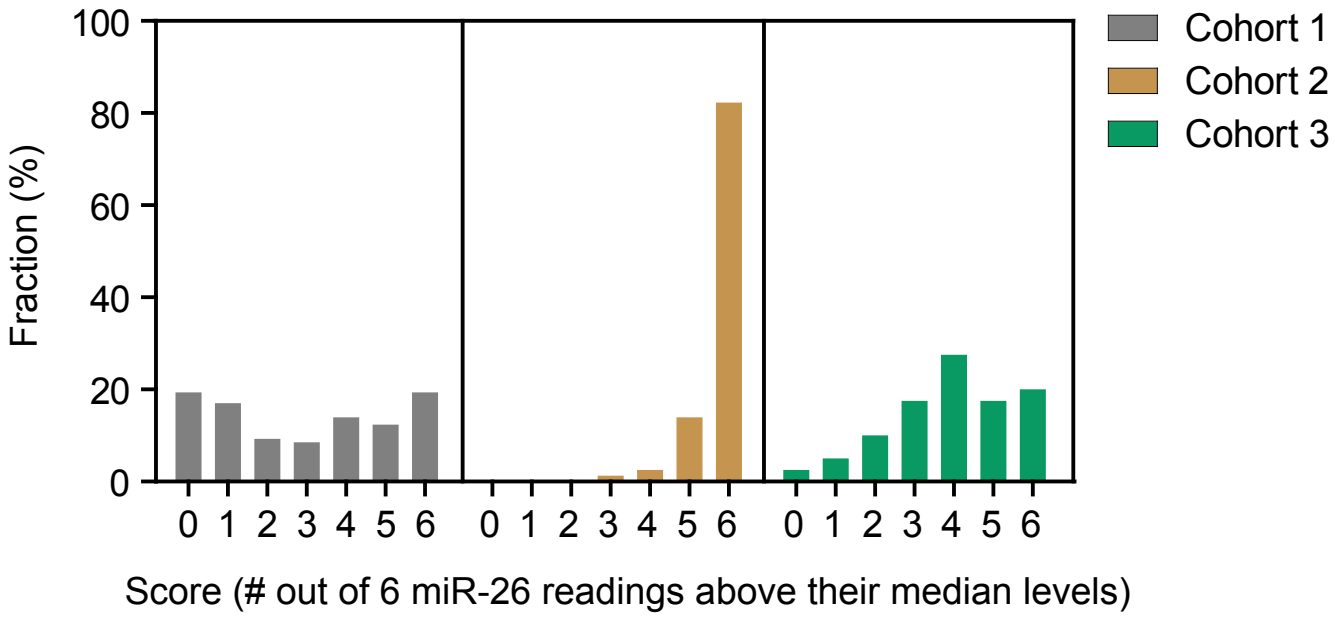


Supplementary Fig 2

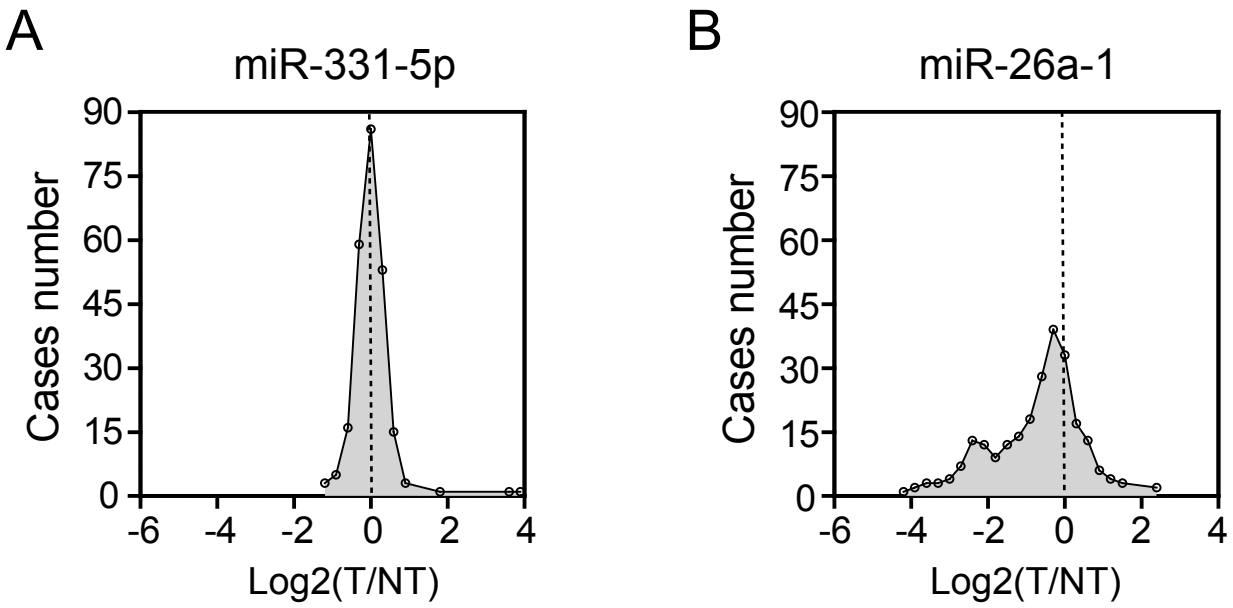
A



B



Supplementary Fig 3



Supplementary table 1. Top 6 miRNAs that are ubiquitously expressed between HCC and non-tumor tissues

Unique id	Mature miR	Median intensity in Non-tumors	Tumor/Non-tumor	
			Median	Variance
hsa-mir-331No2	miR-331-5p	5016.62	0.99	0.26
hsa-mir-371No1	miR-371-3p	3585.02	0.98	0.27
hsa-mir-138-2-prec	miR-138	512.47	1.05	0.50
hsa-mir-323No2	miR-323-5p	659.20	1.01	0.52
hsa-mir-326No2	miR-326-prec	774.34	1.05	0.53
hsa-mir-126No1	miR-126	1492.04	1.06	0.70

[a] The analysis was performed on 241 HCC tumor tissues and their paired adjacent liver tissues with available microRNA array data using paired t-test. P>0.50; Median intensities in non-tumor tissues for each probe > median intensities of entire array.

Supplementary Table 2. Relative expression and variance of eight genes in non-tumor and tumor HCC tissues from three cohorts[a].

Genes	Mean of relative copy numbers (2.5%-97.5%)[b]		
	Non-Tumor	Tumor	P-Value[c]
Cohort 1			
Endogenous controls			
miR-331-5p	7.60 (5.11-8.90)	7.67 (4.98-9.45)	0.640
RNU38b	7.83 (2.06-10.01)	7.62 (1.84-10.24)	0.472
U6B	7.75 (1.30-10.19)	7.91 (1.30-10.93)	0.628
RNU24	8.85 (2.01-11.45)	9.04 (1.91-12.35)	0.589
RNU44	10.20 (3.66-12.98)	10.51 (1.90-14.51)	0.440
U6SnRNA	12.06 (2.81-16.04)	12.41 (4.63-16.88)	0.469
Tested miRs			
miR-26a	12.08 (4.97-15.19)	11.18 (3.84-15.26)	0.034
miR-26b	12.31 (5.17-15.32)	11.47 (3.92-15.66)	0.047
Cohort 2			
Endogenous controls			
miR-331-5p	8.40 (7.27-9.44)	8.37 (7.27-9.57)	0.715
RNU38b	7.74 (6.21-9.14)	7.91 (6.70-9.58)	0.171
U6B	8.12 (6.63-9.52)	8.43 (6.84-10.16)	0.140
RNU44	10.20 (7.45-12.23)	11.02 (8.52-13.89)	<0.001
RNU24	8.58 (5.17-10.58)	9.02 (6.40-11.80)	0.034
U6SnRNA	12.78 (9.88-14.87)	13.15 (9.28-16.04)	0.159
Tested miRs			
miR-26a	14.45 (13.24-15.65)	13.94 (12.33-15.33)	<0.001
miR-26b	14.85 (13.69-16.10)	14.50 (13.06-16.04)	0.002
Cohort 3			
Endogenous controls			
miR-331-5p	6.52 (4.39-7.65)	6.61 (5.61-7.36)	0.487
RNU38b	6.98 (2.15-8.65)	7.47 (3.08-9.13)	0.076
U6B	6.08 (1.89-7.70)	6.54 (0.91-8.35)	0.123
RNU44	9.75 (3.35-12.35)	10.82 (3.13-14.42)	0.065
RNU24	8.27 (2.46-10.71)	8.84 (1.67-11.67)	0.135
U6SnRNA	12.38 (2.69-15.92)	12.99 (3.71-16.53)	0.297
Tested miRs			
miR-26a	12.53 (5.37-14.52)	12.35 (5.89-14.47)	0.656
miR-26b	10.98 (3.30-12.90)	10.92 (4.18-13.15)	0.885

[a] There are three cohorts involved in this study. Cohort 1: Tumor (n=129); Non-tumor (N=100). Cohort 2: Tumor (n=79); Non-tumor (n=79). Cohort 3: Tumor (n=40); Non-tumor (n=40).

[b] Relative copy numbers were in log(2) scale. The formula is Relative copy number = 36-Ct Value.

[c] Unpaired t-test.

Supplementary Table 3. Comparison of Clinical Characteristics between Low miR-26 cases and high miR-26 cases in three independent cohorts[a].

Clinical variable	Cohort 1			Cohort 2			Cohort 3		
	Low miR-26 (n=88)	High miR-26 (n=41)	*p*-value	Low miR-26 (n=3)	High miR-26 (n=76)	*p*-value	Low miR-26 (n=25)	High miR-26 (n=15)	*p*-value
Gender									
Female	6	6		0	14		2	2	
Male	82	35	*0.155*[b]	3	62	*0.155*[b]	23	13	*0.587*[b]
Age-year									
Median (range)	51 (29-77)	48 (20-76)	*0.227*[b]	52 (48-66)	52 (24-75)	*0.774*[b]	66 (54-81)	65 (55-73)	*0.949*[b]
Alanine transaminase (ALT)									
Normal (≤50U/L)	72	36		1	43		7	3	
Abnormal (>50U/L)	12	5	*0.749*[b]	2	33	*0.427*[b]	18	12	*0.572*[b]
Missing data	4	0		0	0		0	0	
HBV									
Negative	5	1		0	9		0	0	
Positive	83	40	*0.664*[b]	3	67	*1.000*[b]	0	0	/
HCV									
Negative	88	41		3	71		0	0	
Positive	0	0	/	0	3	*0.722*[b]	25	15	/
Missing data	0	0		0	2		0	0	
Tumor size-cm									
<=3	56	24		1	21		17	8	
>3	32	17	*0.578*[b]	2	55	*0.829*[b]	8	7	*0.354*[b]
Multinodular									
No	75	35		2	61		21	12	
Yes	13	6	*0.984*[b]	1	15	*0.566*[b]	4	3	*0.747*[b]
TNM Stage									
I	51	28		0	7		6	1	
II	18	10		0	34		13	11	
III-IV	11	3	*0.588*[b]	3	35	*0.186*[b]	6	3	*0.303*[b]
Missing data	8	0		0	0		0	0	
Alpha fetoprotein (AFP)									
Negative (≤20ng/ml)	32	17		1	32		17	11	
Positive (>20ng/ml)	56	24	*0.578*[b]	2	44	*0.763*[b]	8	4	*0.722*[b]
Survival-month									
Median (range)	37 (2-119)	45 (6-116)	*0.058*[c]	9 (9)	>116 (5-116)	*0.034*[c]	76 (50-145)	85 (51-157)	*0.835*[c]

[a]Low miR-26 and high miR-26 groups were assigned by miR-26DX; [b]Chi-square test; [c]Log-rank test