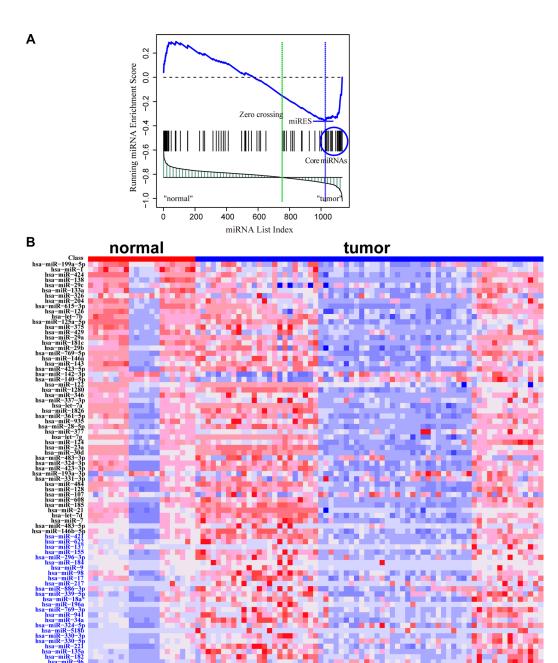
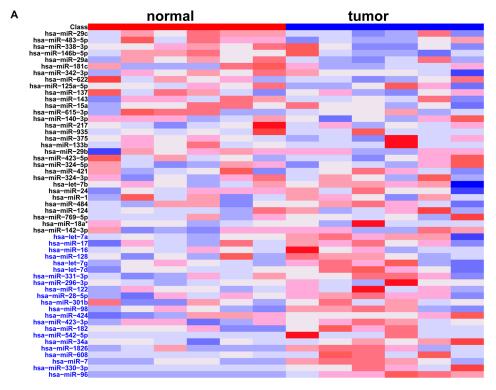
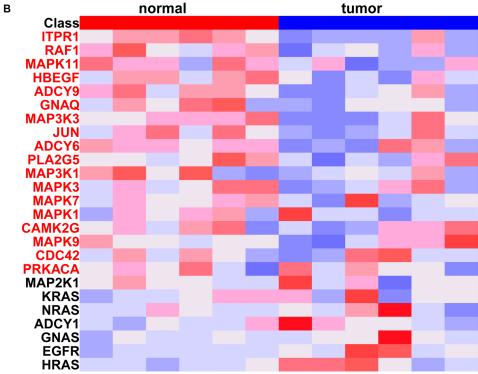
## MiRSEA: Discovering the pathways regulated by dysfunctional MicroRNAs

**Supplementary Materials** 

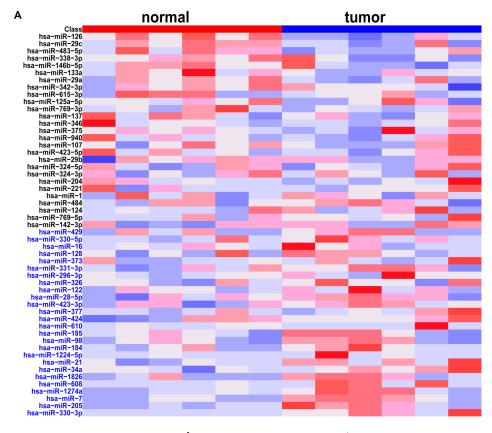


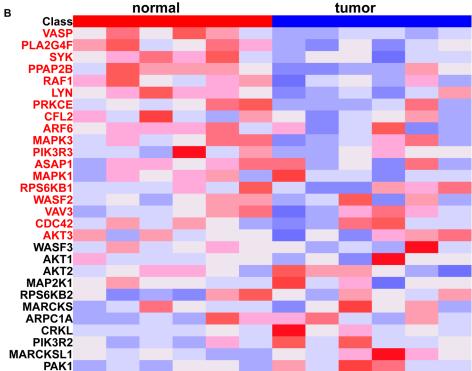
**Supplementary Figure S1: Running enrichment score of the chemokine signaling pathway.** (A) Running-sum statistic is calculated by walking down the miRNA list, and the maximum deviation from zero of the statistic is used as miRNA enrichment score (miRES) of the pathway. (B) Heatmap of the miRNAs in the pathway. Core miRNAs are marked with blue.



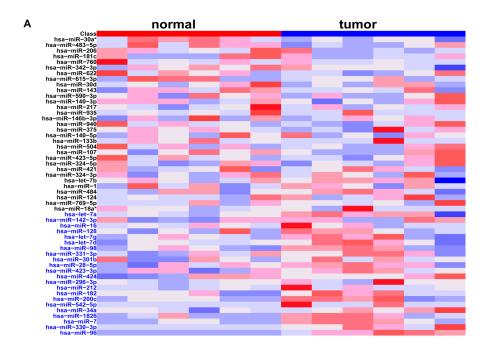


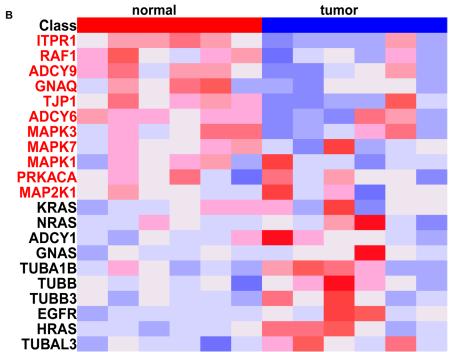
**Supplementary Figure S2:** (A) Heatmap of the miRNAs in the GnRH signaling pathway. Core miRNAs are marked with blue. (B) Heatmap of the mRNAs targeted by core miRNAs in the pathways. Down-regulated genes in the NSCLC samples are marked with red.





**Supplementary Figure S3:** (A) Heatmap of the miRNAs in the Fc gamma R-mediated phagocytosis pathway. Core miRNAs are marked with blue. (B) Heatmap of the mRNAs targeted by core miRNAs in the pathways. Down-regulated genes in the NSCLC samples are marked with red.





**Supplementary Figure S4:** (A) Heatmap of the miRNAs in the gap junction pathway. Core miRNAs are marked with blue. (B) Heatmap of the mRNAs targeted by core miRNAs in the pathways. Down-regulated genes in the NSCLC samples are marked with red.

Supplementary Table S1: Full list of ranked KEGG pathways identified by MiRSEA in the human hepatocellular carcinoma (HCC) dataset. See Supplementary\_Table\_S1.

Supplementary Table S2: Detail information for each miRNA in the sphingolipid metabolism pathway

#	miRNA	LIST LOC	miRSCORE	RES	CORE_ENRICHMENT	
1	hsa-miR-1	4	0.898	0.223	YES	
2	hsa-miR-125b	8	0.785	0.418	YES	
3	hsa-miR-615-3p	9	0.781	0.615	YES	
4	hsa-miR-375	20	0.643	0.768	YES	
5	hsa-miR-769-5p	68	0.463	0.842	YES	
6	hsa-miR-423-3p	757	-0.00093	0.23	NO	
7	hsa-miR-331-3p	766	-0.0103	0.226	NO	
8	hsa-miR-484	783	-0.0274	0.219	NO	
9	hsa-miR-128	818	-0.0533	0.202	NO	
10	hsa-miR-98	1065	-0.312	0.0614	NO	

**Supplementary Table S3: Detail information for each miRNA in the chemokine signaling pathway.** See Supplementary Table S3.

Supplementary Table S4: Full list of ranked KEGG pathways identified by MiRSEA in the gastric adenocarcinoma dataset. See Supplementary\_Table\_S4.

Supplementary Table S5: Detail information for each miRNA in the leukocyte transendothelial migration pathway

#	miRNA	LIST LOC	miRSCORE	RES	CORE_ENRICHMENT
1	hsa-miR-204	1	1.24	0.122	YES
2	hsa-miR-133a	2	0.816	0.202	YES
3	hsa-miR-193a-3p	3	0.762	0.277	YES
4	hsa-miR-338-3p	4	0.676	0.343	YES
5	hsa-miR-610	5	0.65	0.407	YES
6	hsa-miR-137	6	0.534	0.459	YES
7	hsa-miR-339-5p	8	0.471	0.503	YES
8	hsa-miR-326	10	0.437	0.543	YES
9	hsa-miR-375	17	0.318	0.558	YES
10	hsa-miR-29c	20	0.298	0.582	YES
11	hsa-miR-142-3p	22	0.274	0.606	YES
12	hsa-miR-1280	23	0.265	0.632	YES
13	hsa-miR-886-3p	25	0.248	0.654	YES
14	hsa-miR-29b	42	0.162	0.626	NO
15	hsa-miR-423-5p	71	0.122	0.562	NO
16	hsa-miR-1	73	0.12	0.571	NO
17	hsa-miR-138	86	0.108	0.548	NO
18	hsa-miR-532-3p	102	0.0894	0.516	NO
19	hsa-miR-769-5p	122	0.0675	0.471	NO
20	hsa-miR-126	123	0.0631	0.477	NO
21	hsa-miR-146a	125	0.0627	0.481	NO
22	hsa-miR-331-3p	143	0.0456	0.439	NO
23	hsa-miR-324-5p	162	0.0272	0.392	NO
24	hsa-miR-29a	167	0.0214	0.383	NO
25	hsa-miR-615-3p	181	0.0135	0.349	NO
26	hsa-miR-30d	186	0.012	0.339	NO
27	hsa-miR-484	206	-0.00507	0.288	NO
28	hsa-miR-24	216	-0.0113	0.264	NO
29	hsa-miR-221	235	-0.0217	0.217	NO
30	hsa-miR-324-3p	248	-0.0306	0.188	NO
31	hsa-miR-342-3p	266	-0.0447	0.146	NO
32	hsa-miR-361-5p	309	-0.0893	0.0396	NO
33	hsa-miR-23a	327	-0.12	0.00494	NO
34	hsa-miR-455-3p	356	-0.166	-0.0553	NO
35	hsa-miR-128	357	-0.168	-0.0388	NO
36	hsa-miR-146b-5p	361	-0.18	-0.0293	NO
37	hsa-miR-155	388	-0.306	-0.0703	NO
38	hsa-miR-183	389	-0.307	-0.0401	NO
39	hsa-miR-1826	396	-0.359	-0.0212	NO
40	hsa-miR-98	403	-0.466	0.0082	NO

**Supplementary Table S6: Detail information for each miRNA in the focal adhesion pathway.** See Supplementary\_Table\_S6.

Supplementary Table S7: Number of significant pathway identified by MiRSEA, Traditional method and Godard et al. method in human hepatocellular carcinoma, gastric adenocarcinoma, oral carcinoma, acute lymphoblastic leukemia and lung cancer datasets

Method	MiRSEA		Traditional method		Godard et al. method	
Dataset	Up	Down	Up	Down	Up	Down
Human hepatocellular carcinoma	11	22	27	33	0	0
Gastric adenocarcinoma	0	15	29	41	0	48
Oral carcinoma	16	1	65	59	49	0
Acute lymphoblastic leukemia	35	12	8	1	0	0
Lung cancer	61	0	56	31	46	0

Supplementary Table S8: Pathways identified by three methods (MiRSEA, Traditional method, Godard et al. method) with FDR < 0.01 in the prostate cancer dataset. See Supplementary\_Table\_S8.