

Figure S2. Visualizing the miRNA network using a heatmap plot in GSE32960. The heatmap describes the TOM among all DEMs in the analysis. Light colour represents a low overlap and a gradually darker colour indicates a higher overlap. Along the diagonal blocks of darker colours are the co-expression modules. The module assignment and gene dendrogram are also presented along the top and the left side. TOM, Topological Overlap Matrix; DEMs, differentially expressed miRNAs.

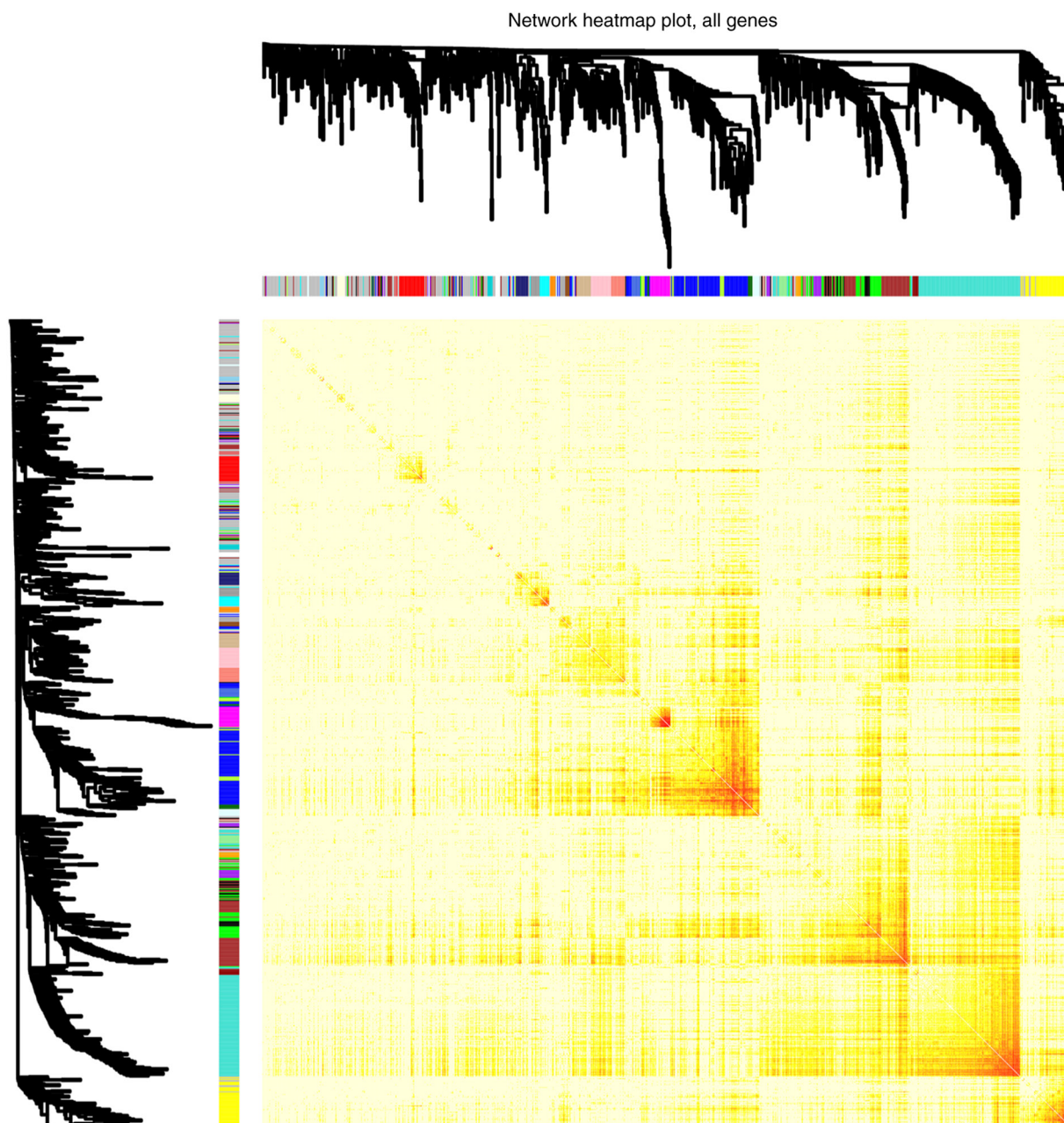


Figure S3. Four DEMs are negatively associated with overall survival in NPC. (A) Patients with a low level of hsa-miR-142-3p (n=200) had a poorer prognosis than those with a high level of hsa-miR-142-3p (n=112) (P=0.0011). (B) The difference in prognosis between patients with a low level of miR-150 (n=190) and those with a high level of hsa-miR-150 (n=122) (P=0.3478) was not significant. (C) Patients with a low level of hsa-miR-29b (n=187) had a poorer prognosis than those with a high level of hsa-miR-29b (n=125) (P=0.0399). (D) Patients with a low level of hsa-miR-29c (n=184) had a poorer prognosis than those with a high level of hsa-miR-29c (n=128) (P=0.013). DEMs, differentially expressed miRNAs; NPC, nasopharyngeal carcinoma; HR, hazard ratio; CI, confidence interval.

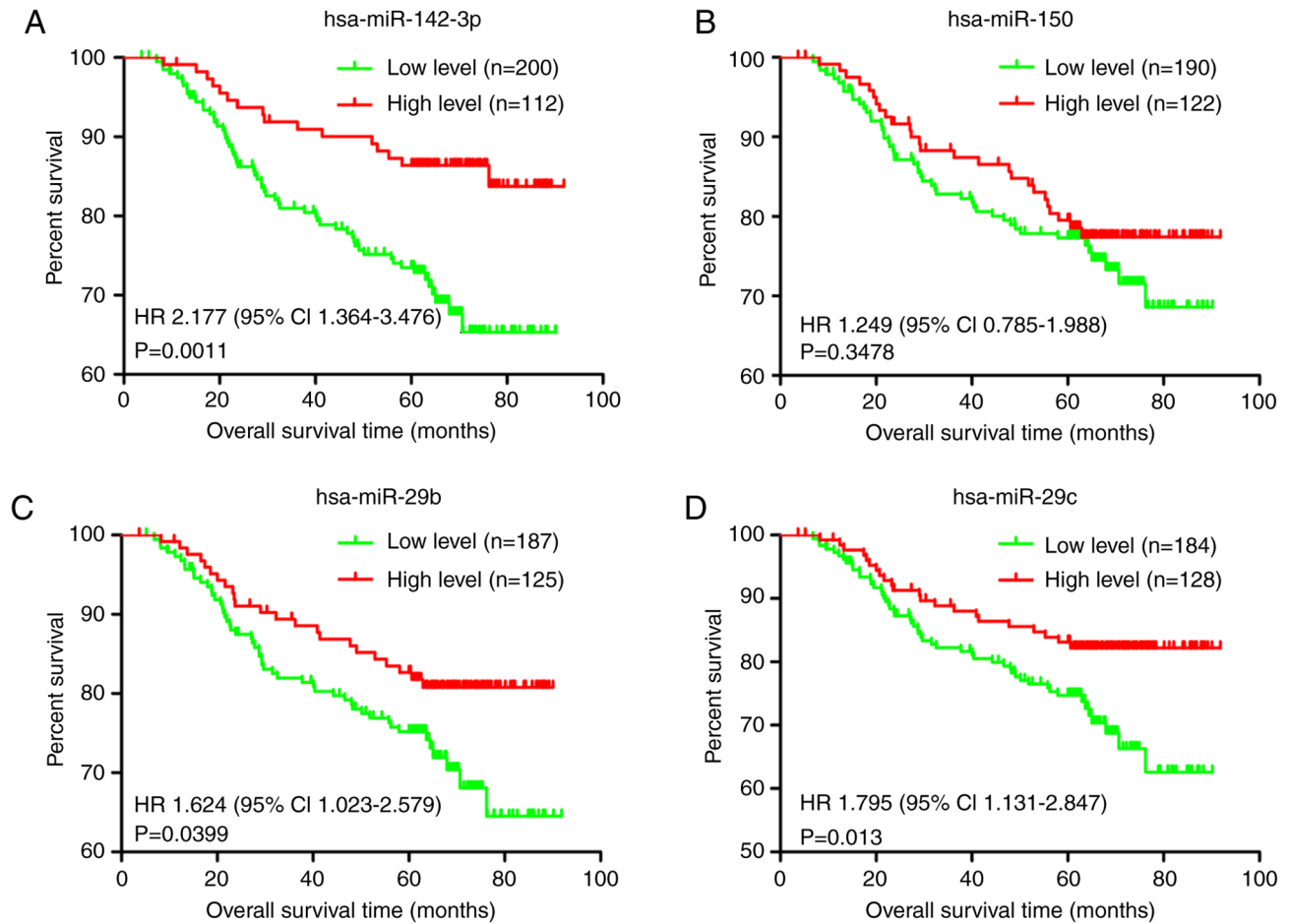


Figure S4. Four DEMs are negatively associated with DFS in NPC. (A) Patients with a low level of hsa-miR-142-3p (n=200) had a poorer prognosis than those with a high level of hsa-miR-142-3p (n=112) (P=0.0004). (B) Patients with a low level of hsa-miR-150 (n=190) had a poorer prognosis than those with a high level of hsa-miR-150 (n=122) (P=0.0471). (C) Patients with a low level of hsa-miR-29b (n=187) had a poorer prognosis than those with a high level of hsa-miR-29b (n=125) (P=0.0466). (D) Patients with a low level of hsa-miR-29c (n=184) had a poorer prognosis than those with a high level of hsa-miR-29c (n=128) (P=0.0012). DEMs, differentially expressed miRNAs; DFS, disease-free survival; NPC, nasopharyngeal carcinoma; HR, hazard ratio; CI, confidence interval.

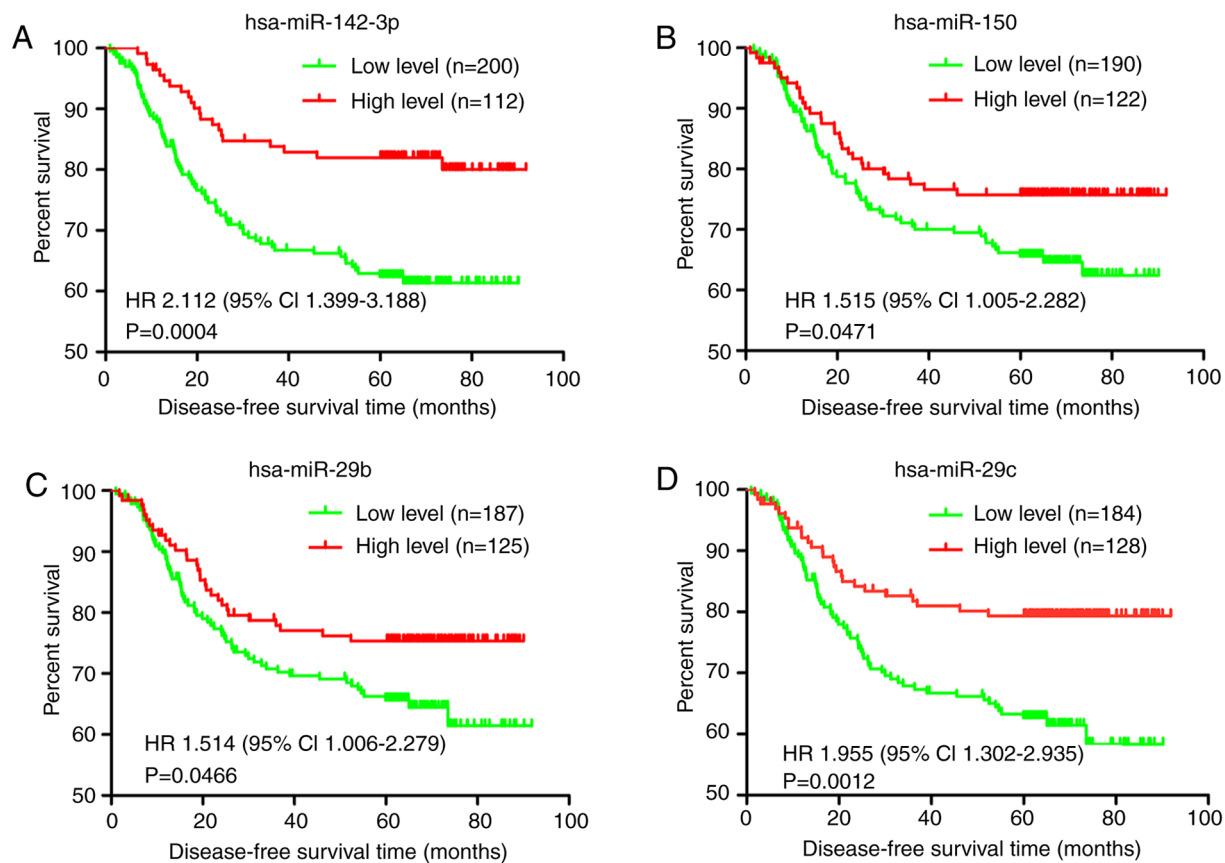


Figure S5. Four DEMs are negatively associated with DMFS in NPC. (A) Patients with a low level of hsa-miR-142-3p (n=200) had a poorer prognosis than those with a high level of hsa-miR-142-3p (n=112) (P=0.0013). (B) The difference in prognosis between patients with a low level of hsa-miR-150 (n=190) and those with a high level of hsa-miR-150 (n=122) (P=0.0615) is not significant. (C) The difference in prognosis between patients with a low level of hsa-miR-29b (n=187) and those with a high level of hsa-miR-29b (n=125) (P=0.6062) is not significant. (D) Patients with a low level of hsa-miR-29c (n=184) had a poorer prognosis than those with a high level of hsa-miR-29c (n=128) (P=0.0041). DEMs, differentially expressed miRNAs; DMFS, distant metastasis-free survival; NPC, nasopharyngeal carcinoma; HR, hazard ratio; CI, confidence interval.

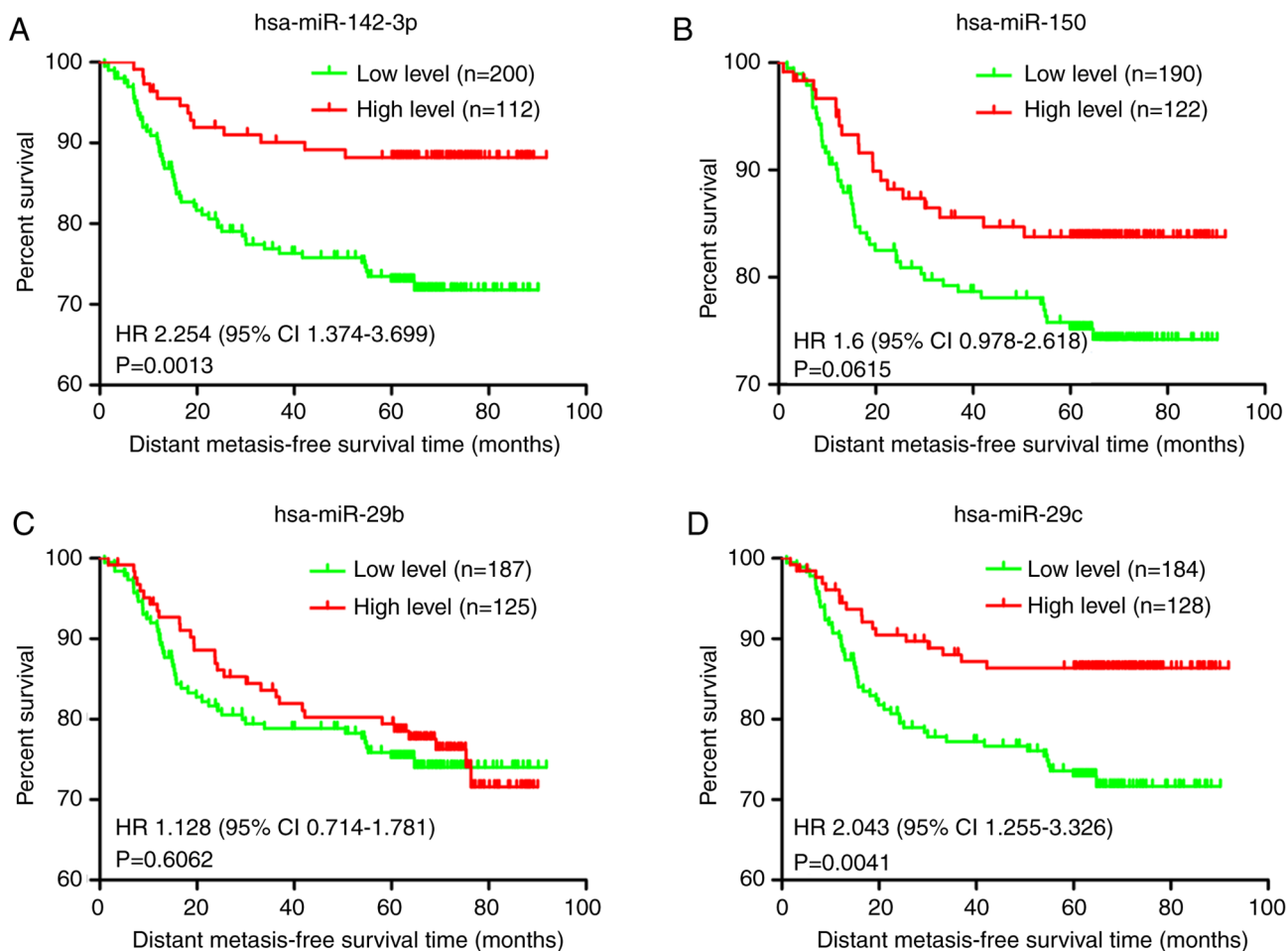


Table SI. Forty-six miRNAs (fold change >2.5, FDR<0.01) differentially expressed in 312 samples of NPC compared with 18 samples of NP.

microRNAs	Fold change	FDR	log ₂ (Fold change)	-log ₁₀ (FDR)
hsa-miR-142-3p	0.107	1.09E-97	-3.220	96.964
hsa-miR-150	0.163	5.24E-88	-2.620	87.281
hsa-miR-29b	0.184	1.19E-77	-2.446	76.925
hsa-let-7f	0.201	1.10E-69	-2.315	68.958
hsa-miR-101	0.256	3.97E-69	-1.964	68.401
hsa-miR-26b	0.287	5.30E-65	-1.800	64.276
hsa-miR-125a-5p	0.270	3.25E-59	-1.888	58.488
hsa-miR-143	0.308	4.85E-53	-1.697	52.315
hsa-let-7i	0.212	1.08E-52	-2.240	51.965
hsa-miR-29c	0.229	5.50E-49	-2.129	48.259
hsa-let-7g	0.293	2.01E-48	-1.773	47.698
hsa-miR-100	0.259	4.17E-47	-1.947	46.380
hsa-miR-30e	0.320	1.67E-46	-1.645	45.777
hsa-miR-342-3p	0.366	2.01E-46	-1.449	45.698
hsa-let-7d	0.256	1.47E-45	-1.965	44.832
hsa-miR-374a	0.390	5.05E-43	-1.358	42.297
hsa-miR-16	0.230	5.28E-36	-2.118	35.277
hsa-miR-142-5p	0.380	2.23E-35	-1.396	34.652
hsa-miR-103	0.311	2.71E-34	-1.684	33.567
hsa-miR-29a	0.280	1.25E-33	-1.835	32.904
hsa-miR-203	0.346	2.51E-32	-1.532	31.601
hsa-miR-26a	0.266	3.28E-30	-1.908	29.484
hsa-miR-22	0.386	9.67E-28	-1.374	27.014
hsa-miR-21	0.326	5.13E-24	-1.615	23.290
hsa-miR-145	0.326	3.68E-22	-1.617	21.435
hsa-miR-99a	0.344	8.15E-22	-1.540	21.089
hsa-miR-19b	0.382	3.52E-17	-1.387	16.453
hsa-miR-34c-5p	0.294	1.09E-13	-1.766	12.964
hsa-miR-30c-2 ^a	2.697	2.45E-12	1.431	11.611
hsa-miR-451	0.315	7.96E-11	-1.666	10.099
hsa-miR-663	2.534	1.40E-09	1.341	8.853
hsa-miR-1238	2.731	4.49E-09	1.450	8.348
hsa-miR-767-5p	7.599	2.41E-08	2.926	7.618
hsa-miR-25 ^a	2.983	1.13E-07	1.577	6.949
hsa-miR-29a ^a	0.363	1.33E-06	-1.462	5.876
hsa-miR-194 ^a	3.167	2.61E-06	1.663	5.584
ebv-miR-BART16	3.270	6.76E-06	1.709	5.170
hsa-miR-15b	0.356	6.96E-06	-1.489	5.158
ebv-miR-BART10	6.218	2.27E-04	2.637	3.644
ebv-miR-BART4-3p	2.579	1.12E-03	1.367	2.950
ebv-miR-BART4	3.256	1.25E-03	1.703	2.904
hsa-miR-93	2.619	1.25E-03	1.389	2.904
hsa-miR-622	3.861	1.63E-03	1.949	2.789
ebv-miR-BART6-3p	3.377	2.33E-03	1.756	2.633
hsa-miR-1197	0.303	3.23E-03	-1.720	2.491
ebv-miR-BART2-5p	3.458	4.75E-03	1.790	2.323

These 46 microRNAs were used in the clustering analysis in Fig. 1B and C (cut-off criteria are fold change >2.5 and P<0.01). NPC, nasopharyngeal carcinoma; NP, normal nasopharyngeal tissue; FDR, false discovery rate. The 'a' symbol belongs to the name of miRNA (an old nomenclature).

Table SII. Eight miRNAs in the dark green module that are correlated with DMFS.

miRNAs in the dark green module	Relationship with the dark green module
hsa-miR-29c	0.852
hsa-miR-29b	0.850
hsa-miR-150	0.841
hsa-miR-142-3p	0.798
hsa-miR-342-3p	0.728
hsa-miR-221	0.576
hsa-miR-222	0.541
hsa-miR-142-5p	0.447

The correlation ranged from 0.447 to 0.852. miRNAs, microRNAs; DMFS, distant metastasis-free survival.

Table SIII. Univariate Cox regression analysis of the 46 differentially expressed miRNAs associated with DMFS in the training set of 312 NPC patients.

miRNAs	β coefficient	HR	CI 95%	P-value
hsa-let-7d	-0.24	0.79	0.58-1.08	0.141
hsa-miR-100	-0.21	0.81	0.56-1.16	0.256
hsa-miR-101	-0.04	0.96	0.57-1.64	0.894
hsa-miR-103	-0.14	0.87	0.66-1.15	0.325
hsa-let-7f	-0.28	0.76	0.55-1.04	0.088
hsa-let-7i	-0.31	0.74	0.55-0.97	0.032 ^b
hsa-miR-143	0.06	1.06	0.65-1.73	0.805
hsa-miR-142-3p	-0.6	0.55	0.4-0.76	<0.0001 ^b
hsa-miR-142-5p	0	1	0.6-1.67	0.988
hsa-miR-150	-0.37	0.69	0.52-0.91	0.009 ^b
hsa-miR-15b	0.14	1.15	0.7-1.91	0.58
hsa-miR-16	-0.13	0.88	0.72-1.08	0.218
hsa-miR-19b	-0.1	0.9	0.67-1.22	0.501
hsa-miR-203	-0.36	0.7	0.37-1.33	0.274
hsa-miR-21	-0.01	0.99	0.82-1.21	0.958
hsa-miR-22	-0.16	0.85	0.56-1.29	0.442
hsa-miR-26a	-0.42	0.66	0.52-0.83	0.001 ^b
hsa-miR-26b	-0.49	0.61	0.33-1.13	0.119
hsa-miR-25 ^a	0.04	1.04	0.74-1.48	0.808
hsa-miR-29a	-0.19	0.83	0.67-1.02	0.083
hsa-miR-29a ^a	0.19	1.2	0.71-2.04	0.492
hsa-miR-29b	-0.42	0.66	0.46-0.93	0.018 ^b
hsa-miR-29c	-0.66	0.52	0.37-0.72	<0.0001 ^b
hsa-miR-30e	-0.79	0.45	0.31-0.66	<0.0001 ^b
hsa-miR-342-3p	-0.31	0.73	0.44-1.23	0.242
hsa-miR-374a	-0.33	0.72	0.39-1.35	0.307
hsa-miR-451	0.3	1.35	1.04-1.75	0.025 ^b
hsa-miR-622	0.14	1.15	0.88-1.51	0.316
hsa-miR-663	0.28	1.33	0.82-2.16	0.251
hsa-miR-767-5p	0.08	1.08	0.9-1.31	0.399
hsa-miR-99a	-0.05	0.96	0.71-1.29	0.767
hsa-miR-93	0.48	1.62	1.14-2.3	0.007 ^b
hsa-miR-145	-0.21	0.81	0.55-1.19	0.286
hsa-let-7g	-0.32	0.73	0.52-1.02	0.064
hsa-miR-30c-2 ^a	0.22	1.24	0.75-2.07	0.403
hsa-miR-125a-5p	0.3	1.35	0.86-2.12	0.188
hsa-miR-34c-5p	-0.12	0.89	0.57-1.38	0.593
hsa-miR-194 ^a	0.1	1.1	0.76-1.6	0.608
hsa-miR-1197	0.28	1.32	0.9-1.94	0.152
hsa-miR-1238	0.09	1.09	0.73-1.62	0.673
ebv-miR-BART10	0.12	1.13	0.86-1.49	0.377
ebv-miR-BART2-5p	0.13	1.14	0.86-1.51	0.375
ebv-miR-BART16	-0.04	0.96	0.66-1.39	0.823
ebv-miR-BART4	0.06	1.06	0.75-1.51	0.732
ebv-miR-BART6-3p	0.05	1.06	0.81-1.38	0.694
ebv-miR-BART4-3p	0.02	1.02	0.73-1.43	0.899

The HRs and P-values were calculated utilizing the unadjusted Cox proportional-hazards model. miRNAs, microRNAs; DMFS, distant metastasis-free survival; NPC, nasopharyngeal, carcinoma; HRs, hazards ratios; CI, confidence interval. The 'a' symbol belongs to the name of miRNA (an old nomenclature). ^bP<0.05, statistically significant.

Table SV. Clinical characteristics of patients according to the risk score of a four-miRNA signature.

Clinical characteristics	High-risk group (n=156)	Low-risk group (n=156)	P-value ^a
Age, years	46.88 (SD:10.99)	46.98 (SD:11.02)	0.94
Sex, male	126 (81%)	107 (69%)	0.013 ^b
WHO pathological type			0.85
Undifferentiated non-keratinizing	151	150	
Differentiated non-keratinizing	4	4	
Keratinizing squamous cell	1	2	
VCA-IgA			0.85
<1:80	21	24	
1:80-1:320	91	87	
≥1:640	43	45	
EA-IgA			0.52
<1:10	36	40	
1:10-1:20	47	53	
≥1:40	73	63	
T stage			0.0052 ^b
T1	26	40	
T2	38	51	
T3	36	35	
T4	56	30	
N stage			0.41
N0	19	25	
N1	78	70	
N2	32	40	
N3	27	21	
TNM stage			0.0037 ^b
I	4	8	
II	38	48	
III	37	54	
IV	77	46	
RT period interruptions			0.25
0 days	84	94	
≥1 day	72	62	
RT boosting			0.91
No	82	81	
Yes	74	75	
Chemotherapy			0.19
No	26	18	
Yes	130	138	
DMFS		<0.0001 ^b	
Distant metastases	63 (40%)	3 (2%)	
5-year	40%	96%	
RFS			<0.0001 ^b
Relapse	31 (20%)	12 (8%)	
5-year	43%	91%	
DFS			<0.0001 ^b
Relapse or death	81 (52%)	14 (9%)	
5-year	38%	91%	
OS			<0.0001 ^b
Death	69 (44%)	5 (3%)	
5-year	43%	97%	

^aχ² test and Student's t-test. miRNA, microRNA; VCA-IgA, viral capsid antigen-immunoglobulin A; EA-IgA, early antigen-immunoglobulin A; RT, radiotherapy; TNM, tumour-node-metastasis; DMFS, distant metastasis-free survival; RFS, relapse-free survival; OS, overall survival.

^bP<0.05, statistically significant.

Table SVI. Summary of the univariate Cox regression analysis of prognostic factors for DMFS in 312 NPC patients.

Variable	Regression coefficient	HR	CI 95%	P-value
Age (≥ 45 years vs. < 45 years)	0.25	1.28	0.78-2.1	0.328
AJCC7 N stage (stage 2-3 vs. 0-1)	0.78	2.18	1.34-3.53	0.002 ^a
AJCC7 T stage (stage III-IV vs. I-II)	1.47	4.36	1.99-9.55	$< 0.0001^a$
AJCC7 TNM stage (stage III-IV vs. I-II)	0.78	2.18	1.3-3.63	0.003 ^a
Concurrent chemotherapy (yes vs. no)	0.04	1.04	0.52-2.11	0.903
EA-IgA ($\geq 1:40$ vs. 1:10-1:20 vs. $< 1:10$)	0.3	1.36	0.98-1.87	0.064
RT boosting (yes vs. no)	-0.13	0.88	0.54-1.43	0.605
RT interrupt (0 day vs. > 1 days)	0.1	1.1	0.68-1.79	0.7
Risk score	2.16	8.68	5.74-13.12	$< 0.0001^a$
Sex (men vs. women)	-0.62	0.54	0.28-1.02	0.059
VCA-IgA ($\geq 1:640$ vs. 1:80-1:320 vs. $< 1:8$)	0.06	1.06	0.72-1.55	0.766
WHO type	-0.23	0.79	0.34-1.83	0.583

The HRs and P-values were calculated using univariate Cox regression analysis. DMFS, distant metastasis-free survival; NPC, nasopharyngeal carcinoma; HR, hazard ratio; CI, confidence interval; TNM, tumour-node-metastasis; EA-IgA, early antigen immunoglobulin A; RT, radiotherapy; VCA-IgA, viral capsid antigen immunoglobulin A. ^aP < 0.05 , statistically significant.

Table SVII. Summary of the multivariable Cox regression analysis of prognostic factors for DMFS and risk score in 312 NPC patients.

Variable	Regression coefficient	HR	CI 95%	P-value
AJCC7 N stage (stage 2-3 vs. 0-1)	0.57	1.76	0.958-3.233	0.068
AJCC7 T stage (stage III-IV vs. I-II)	0.78	2.18	1.085-4.393	0.029 ^a
AJCC7 TNM stage (stage III-IV vs. I-II)	0.22	1.24	0.417-3.715	0.695
EA-IgA ($\geq 1:40$ vs. 1:10-1:20 vs. $< 1:10$)	0.09	1.1	0.784-1.53	0.595
Risk score	2.4	11.02	6.58-18.463	$< 0.0001^a$
Sex (men vs. women)	-0.2	0.82	0.424-1.586	0.555

The HRs and P-values were calculated through an adjusted multivariate Cox regression analysis, including risk score (high risk vs. low risk), AJCC7 N stage (stage 2-3 vs. 0-1), AJCC7 T stage (stage III-IV vs. I-II), AJCC7 TNM stage (stage III-IV vs. I-II), EA-IgA ($\geq 1:40$ vs. 1:10-1:20 vs. $< 1:10$), sex; DMFS, distant metastasis-free survival; NPC, nasopharyngeal carcinoma; EA-IgA, early antigen-immunoglobulin A. ^aP < 0.05 , statistically significant.

Table SVIII. The 127 upregulated mRNAs (fold change >1.5, FDR <0.05) differentially expressed between 31 NPC samples and 10 normal samples.

Gene symbol	FDR	logFC	Gene title
NID1	4.81E-09	2.23	Nidogen 1
COL4A2	5.03E-08	2.19	Collagen type IV α 2 chain
COL4A1	6.52E-08	2.39	Collagen type IV α 1 chain
FMNL2	1.16E-06	1.63	Formin like 2
SPARC	3.85E-06	1.85	Secreted protein acidic and cysteine rich
COL1A1	4.57E-06	2.62	Collagen type I α 1 chain
CASK	6.29E-06	1.25	Calcium/calmodulin dependent serine protein kinase
SCML2	1.53E-05	0.78	Sex comb on midleg-like 2 (<i>Drosophila</i>)
NRAS	1.64E-05	0.70	Neuroblastoma RAS viral oncogene homolog
NAV1	1.92E-05	0.65	Neuron navigator 1
COL5A1	4.72E-05	0.94	Collagen type V α 1 chain
FBN1	5.79E-05	1.57	Fibrillin 1
AKT3	7.07E-05	1.42	AKT serine/threonine kinase 3
GGCT	7.63E-05	1.09	γ -Glutamylcyclotransferase
CDC7	8.24E-05	1.17	Cell division cycle 7
NUCKS1	1.01E-04	1.00	Nuclear casein kinase and cyclin dependent kinase substrate 1
HOXA10	1.23E-04	1.36	Homeobox A10
COL3A1	1.30E-04	2.27	Collagen type III α 1 chain
TAF5	1.34E-04	0.66	TATA-box binding protein associated factor 5
CBX2	1.38E-04	0.76	Chromobox 2
CYCS	1.72E-04	0.93	Cytochrome c, somatic
TDG	1.74E-04	0.85	Thymine DNA glycosylase
TRA2B	1.79E-04	0.64	Transformer 2 β homolog (<i>Drosophila</i>)
CTDSPL2	1.81E-04	0.73	CTD small phosphatase like 2
CCND2	1.95E-04	1.54	Cyclin D2
ABCE1	2.32E-04	0.99	ATP binding cassette subfamily E member 1
RHEB	3.07E-04	0.83	Ras homolog enriched in brain
CAPRN1	3.25E-04	1.09	Cell cycle associated protein 1
SENPI	3.41E-04	0.92	SUMO1/sentrin specific peptidase 1
MAPRE1	3.53E-04	0.74	Microtubule associated protein RP/EB family member 1
SUB1	3.84E-04	1.32	SUB1 homolog, transcriptional regulator
VASH2	3.98E-04	2.66	Vasohibin 2
EIF2S2	4.07E-04	0.85	Eukaryotic translation initiation factor 2 subunit beta
GPATCH2	4.07E-04	1.04	G-patch domain containing 2
MTR	4.69E-04	0.86	5-Methyltetrahydrofolate-homocysteine methyltransferase
E2F3	4.85E-04	1.04	E2F transcription factor 3
LAMC1	5.21E-04	1.04	Laminin subunit gamma 1
BOD1	5.33E-04	0.89	Biorientation of chromosomes in cell division 1
CAND1	5.60E-04	1.15	Cullin associated and neddylation dissociated 1
MSL1	6.73E-04	0.67	Male specific lethal 1 homolog
OSTC	7.75E-04	0.64	Oligosaccharyltransferase complex non-catalytic subunit
SDC2	8.13E-04	1.38	Syndecan 2
COL15A1	8.40E-04	1.55	Collagen type XV α 1 chain
SCML1	9.17E-04	1.06	Sex comb on midleg-like 1 (<i>Drosophila</i>)
KDELC1	1.01E-03	0.83	KDEL motif containing 1
ADA	1.06E-03	1.56	Adenosine deaminase
NUDCD1	1.18E-03	0.92	NudC domain containing 1
ITGAV	1.24E-03	1.12	Integrin subunit α V
SCAI	1.31E-03	1.46	Suppressor of cancer cell invasion
FLVCR1	1.55E-03	1.21	Feline leukemia virus subgroup C cellular receptor 1
PMP22	1.57E-03	0.75	Peripheral myelin protein 22
EIF4E2	1.73E-03	0.73	Eukaryotic translation initiation factor 4E family member 2
PA2G4	1.74E-03	0.87	Proliferation-associated 2G4
RPRD1A	1.95E-03	0.82	Regulation of nuclear pre-mRNA domain containing 1A
USP31	2.10E-03	1.32	Ubiquitin specific peptidase 31
MAT2A	2.12E-03	0.60	Methionine adenosyltransferase 2A
PMAIP1	2.26E-03	1.98	Phorbol-12-myristate-13-acetate-induced protein 1
FRAS1	2.29E-03	1.75	Fraser extracellular matrix complex subunit 1

Table SVIII. Continued.

Gene symbol	FDR	logFC	Gene title
CALU	2.31E-03	0.74	Calumenin
AMOTL1	2.34E-03	1.02	Angiomotin like 1
XPO1	2.47E-03	0.69	Exportin 1
ZNF267	2.48E-03	0.87	Zinc finger protein 267
TMEM33	2.55E-03	0.71	Transmembrane protein 33
SLC39A10	2.77E-03	0.91	Solute carrier family 39 member 10
ATL2	2.96E-03	1.13	Atlantin GTPase 2
DHTKD1	3.07E-03	0.68	Dehydrogenase E1 and transketolase domain containing 1
HNRNPU	3.08E-03	0.79	Heterogeneous nuclear ribonucleoprotein U
BLMH	3.26E-03	0.71	Bleomycin hydrolase
ACSL4	3.71E-03	0.87	Acyl-CoA synthetase long-chain family member 4
SLC16A1	3.73E-03	1.34	Solute carrier family 16 member 1
PPP3R1	4.19E-03	0.60	Protein phosphatase 3 regulatory subunit B, α
RCHY1	4.25E-03	0.67	Ring finger and CHY zinc finger domain containing 1
MMD	4.74E-03	1.01	Monocyte to macrophage differentiation associated
SIKE1	4.97E-03	0.89	Suppressor of IKBKE 1
ROBO1	5.17E-03	1.16	Roundabout guidance receptor 1
ADAM12	5.37E-03	0.88	ADAM metallopeptidase domain 12
UBFD1	5.40E-03	0.68	Ubiquitin family domain containing 1
NUP160	5.70E-03	0.77	Nucleoporin 160
ADIPOR2	6.68E-03	0.69	Adiponectin receptor 2
PRLR	6.83E-03	1.50	Prolactin receptor
ISG20L2	6.92E-03	0.70	Interferon stimulated exonuclease gene 20 like 2
TET1	7.01E-03	0.59	Tet methylcytosine dioxygenase 1
DCAF6	7.03E-03	0.80	DDB1 and CUL4 associated factor 6
PTEN	7.24E-03	0.65	Phosphatase and tensin homolog
MBTD1	7.26E-03	0.87	Mbt domain containing 1
RPS15A	7.44E-03	0.75	Ribosomal protein S15a
PLXNA1	7.62E-03	0.79	Plexin A1
RNF165	8.25E-03	1.08	Ring finger protein 165
ARPP19	8.40E-03	0.85	cAMP regulated phosphoprotein 19
WTAP	1.04E-02	0.61	Wilms tumor 1 associated protein
KDEL2	1.13E-02	0.60	KDEL endoplasmic reticulum protein retention receptor 2
TNRC6A	1.14E-02	0.79	Trinucleotide repeat containing 6A
PDHX	1.19E-02	0.72	Pyruvate dehydrogenase complex component X
UBE2W	1.25E-02	0.61	Ubiquitin conjugating enzyme E2 W (putative)
SYNCRIP	1.28E-02	0.66	Synaptotagmin binding cytoplasmic RNA interacting protein
COMMD2	1.29E-02	0.68	COMM domain containing 2
SERBP1	1.40E-02	0.76	SERPINE1 mRNA binding protein 1
FBXO45	1.40E-02	0.76	F-box protein 45
TADA1	1.47E-02	0.63	Transcriptional adaptor 1
CCNT2	1.50E-02	0.74	Cyclin T2
SS18L1	1.62E-02	0.71	SS18L1, nBAF chromatin remodeling complex subunit
CCDC117	1.65E-02	0.72	Coiled-coil domain containing 117
SPRED1	1.71E-02	0.76	Sprouty related EVH1 domain containing 1
COL7A1	1.80E-02	0.74	Collagen type VII α 1 chain
CDC73	1.83E-02	0.62	Cell division cycle 73
RFX7	1.87E-02	0.71	Regulatory factor X7
CHSY1	1.98E-02	0.65	Chondroitin sulfate synthase 1
LPL	2.14E-02	1.47	Lipoprotein lipase
PXDN	2.16E-02	1.20	Peroxidasin
WASF1	2.21E-02	0.81	WAS protein family member 1
IREB2	2.30E-02	0.60	Iron responsive element binding protein 2
CLIC4	2.40E-02	0.78	Chloride intracellular channel 4
SCD	2.43E-02	0.94	Stearoyl-CoA desaturase
ATP2B4	2.80E-02	0.62	ATPase plasma membrane Ca ²⁺ transporting 4
NUFIP2	2.87E-02	0.59	NUFIP2, FMR1 interacting protein 2
DCUN1D4	3.37E-02	0.79	Defective in cullin neddylation 1 domain containing 4
LRP6	3.48E-02	0.92	LDL receptor related protein 6

Table SVIII. Continued.

Gene symbol	FDR	logFC	Gene title
USP37	3.58E-02	0.60	Ubiquitin specific peptidase 37
TMTC3	3.83E-02	0.91	Transmembrane and tetratricopeptide repeat containing 3
METAP2	4.09E-02	0.66	Methionyl aminopeptidase 2
ABCA1	4.11E-02	0.60	ATP binding cassette subfamily A member 1
CA2	4.20E-02	0.67	Carbonic anhydrase 2
CPS1	4.33E-02	0.76	Carbamoyl-phosphate synthase 1
QKI	4.45E-02	0.67	QKI, KH domain containing RNA binding
HMGA2	4.54E-02	1.06	High mobility group AT-hook 2
TNFAIP3	4.56E-02	0.81	TNF- α induced protein 3
RHOBTB3	4.69E-02	0.85	Rho related BTB domain containing 3

FDR, false discovery rate; NPC, nasopharyngeal carcinoma.

Table SIX. Summary of major implicated pathways of 127 screened genes.

Term	P-value	Fold Enrichment	Count	Genes
PI3K/Akt signaling pathway	2.69E-06	4.90	14	NRAS, COL4A2, COL4A1, PRLR, CCND2, ITGAV, COL3A1, RHEB, COL1A1, LAMC1, PTEN, EIF4E2, COL5A1, AKT3
Small cell lung cancer	4.87E-06	11.36	8	COL4A2, E2F3, COL4A1, ITGAV, CYCS, LAMC1, PTEN, AKT3
Focal adhesion	3.63E-05	5.86	10	COL4A2, COL4A1, CCND2, ITGAV, COL3A1, COL1A1, LAMC1, PTEN, AKT3, COL5A1
ECM-receptor interaction	6.73E-05	9.71	7	COL4A2, COL4A1, ITGAV, COL3A1, COL1A1, LAMC1, COL5A1
Protein digestion and absorption	7.18E-05	9.60	7	COL4A2, COL4A1, COL7A1, COL3A1, COL15A1, COL1A1, COL5A1
Amoebiasis	1.62E-03	6.83	6	COL4A2, COL4A1, COL3A1, COL1A1, LAMC1, COL5A1
p53 signaling pathway	2.06E-03	9.01	5	CCND2, CYCS, RCHY1, PMAIP1, PTEN
mTOR signaling pathway	1.15E-02	8.32	4	RHEB, PTEN, AKT3, EIF4E2
Pathways in cancer	1.35E-02	2.76	9	NRAS, COL4A2, E2F3, COL4A1, ITGAV, CYCS, LAMC1, PTEN, AKT3
Glioma	1.56E-02	7.43	4	NRAS, E2F3, PTEN, AKT3
Melanoma	1.98E-02	6.80	4	NRAS, E2F3, PTEN, AKT3
Prolactin signaling pathway	1.98E-02	6.80	4	NRAS, PRLR, CCND2, AKT3
Hepatitis B	2.99E-02	4.16	5	NRAS, E2F3, CYCS, PTEN, AKT3
Prostate cancer	3.45E-02	5.49	4	NRAS, E2F3, PTEN, AKT3
Choline metabolism in cancer	4.87E-02	4.78	4	NRAS, WASF1, RHEB, AKT3

Table SX. The top 20 GO terms of 127 screened genes.

Category	Term	P-value	Fold Enrichment	Count	Genes
BP	Extracellular matrix organization	1.73E-07	8.426898628	12	COL4A2, PXDN, COL4A1, COL7A1, ITGAV, COL3A1, FBN1, NID1, COL1A1, SPARC, LAMC1, COL5A1
BP	Collagen catabolic process	6.59E-06	15.05430328	7	COL4A2, COL4A1, COL7A1, COL3A1, COL15A1, COL1A1,
BP	Endodermal cell differentiation	9.41E-04	20.39101396	4	COL4A2, COL7A1, ITGAV, HMGA2
BP	Blood vessel development	0.002562	14.48835203	4	ITGAV, COL1A1, COL5A1, FLVCR1
BP	Cell division	0.003846	3.539297424	9	CDC7, CCNT2, BOD1, CCND2, ARPP19, USP37, CDC73, MAPRE1,
BP	Response to drugs	0.006493	3.622088007	8	XPO1, LPL, BLMH, COL1A1, ABCA1, CPS1, PTEN, ADA
BP	Negative regulation of translation	0.008442	9.49236857	4	IREB2, SYNCRIP, CAPRIN1, EIF4E2
BP	Covalent chromatin modification	0.009038	6.090236472	5	MBTD1, TDG, CBX2, TET1, SS18L1
BP	Heart development	0.010475	4.512765386	6	ROBO1, COL3A1, FBN1, ADIPOR2, SPARC, PTEN
CC	Extracellular matrix	1.59E-08	7.329472329	15	FRAS1, LPL, COL4A2, PXDN, COL4A1, COL3A1, FBN1, COL15A1, RPS15A, NID1, HNRNPU, COL5A1, COL7A1, COL1A1, LAMC1
CC	Basement membrane	6.79E-08	16.47739602	9	FRAS1, COL4A1, COL7A1, FBN1, CASK, NID1, SPARC, LAMC1,
CC	Endoplasmic reticulum lumen	3.62E-04	6.026455026	8	COL4A2, KDELC1, COL4A1, COL7A1, COL3A1, COL15A1,
CC	Nucleoplasm	0.003605	1.662470352	32	CCNT2, XPO1, E2F3, TRA2B, PPP3R1, RPS15A, SYNCRIP, CBX2, CDC73, TADA1, WTAP, PTEN, SPRED1, RCHY1, TNRC6A, RPRD1A, AKT3, CDC7, TAF5, SCAI, ARPP19, ISG20L2, HMGA2, HNRNPU, CTDSPL2, PA2G4, SENP1, CCND2, MSL1, TDG, CAND1, ADAM12
CC	Collagen trimer	0.003702	7.860593513	5	COL7A1, COL3A1, COL15A1, COL1A1, COL5A1
CC	Cell surface	0.012401	2.668540971	10	LPL, PRLR, ROBO1, CLIC4, ITGAV, LRP6, SPARC, HNRNPU, ADA,
MF	Extracellular matrix structural constituent	2.88E-08	18.2870727	9	COL4A2, PXDN, COL4A1, COL3A1, FBN1, COL15A1, COL1A1, LAMC1, COL5A1
MF	Platelet-derived growth factor	5.97E-05	49.50439883	4	COL4A1, COL3A1, COL1A1, COL5A1
MF	Protein binding	3.54E-04	1.301709292	84	CCNT2, XPO1, E2F3, ATL2, WASF1, CASK, SYNCRIP, CBX2, PMAIP1, AMOTL1, WTAP, PTEN, SDC2, ATP2B4, NUDCD1, ROBO1, QKI, SPRED1, RPRD1A, SS18L1, AKT3, FLVCR1, CDC7, ABCE1, CYCS, SCAI, ISG20L2, HMGA2, HNRNPU, BLMH, PA2G4, SENP1, SIKE1, CLIC4, CCND2, SERBP1, EIF2S2, UBE2W, COMM2D2, CAND1, CA2, MAPRE1, COL1A1, PMP22, TNFAIP3, DCUN1D4, OSTC, NUP160, TRA2B, COL3A1, PPP3R1, RPS15A, CDC73, ABCA1, NUFIP2, ADA, CALU, COL7A1, TMEM33, ITGAV, HOXA10, USP37, RCHY1, PDHX, TNRC6A, FBXO45, RHOBTB3, LPL, COL4A2, COL4A1, MAT2A, SUB1, TAF5, FBN1, IREB2, SPARC, CPS1, PRLR, MTR, TDG, LRP6, TMTC3, CCDC117, EIF4E2
MF	Poly(A) RNA binding	0.003376	2.170476299	18	METAP2, NUCKS1, SUB1, TRA2B, RPS15A, SYNCRIP, ISG20L2, NUFIP2, HNRNPU, CAPRIN1, PA2G4, UBF1, SERBP1, EIF2S2, QKI, MAPRE1, TNRC6A, EIF4E2
MF	Apolipoprotein	0.004525	29.17223502	3	LPL, LRP6, ABCA1

GO, Gene ontology; BP, biological process; CC, cellular component; MF, molecular function.