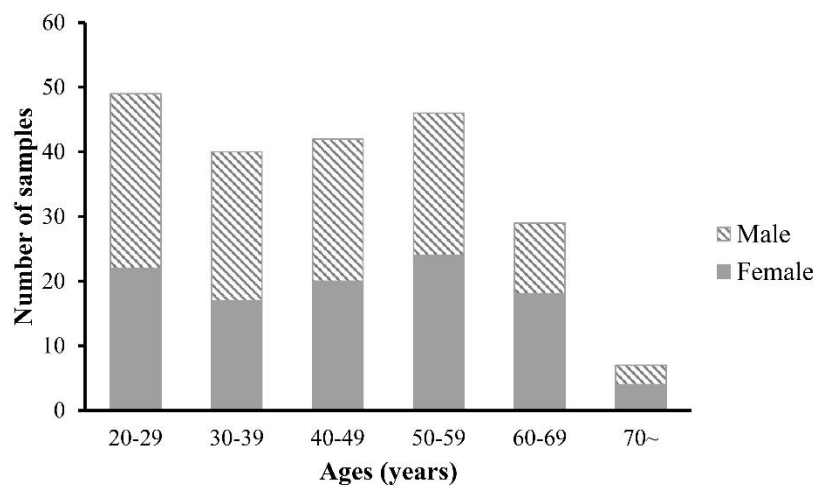


Supplementary Material

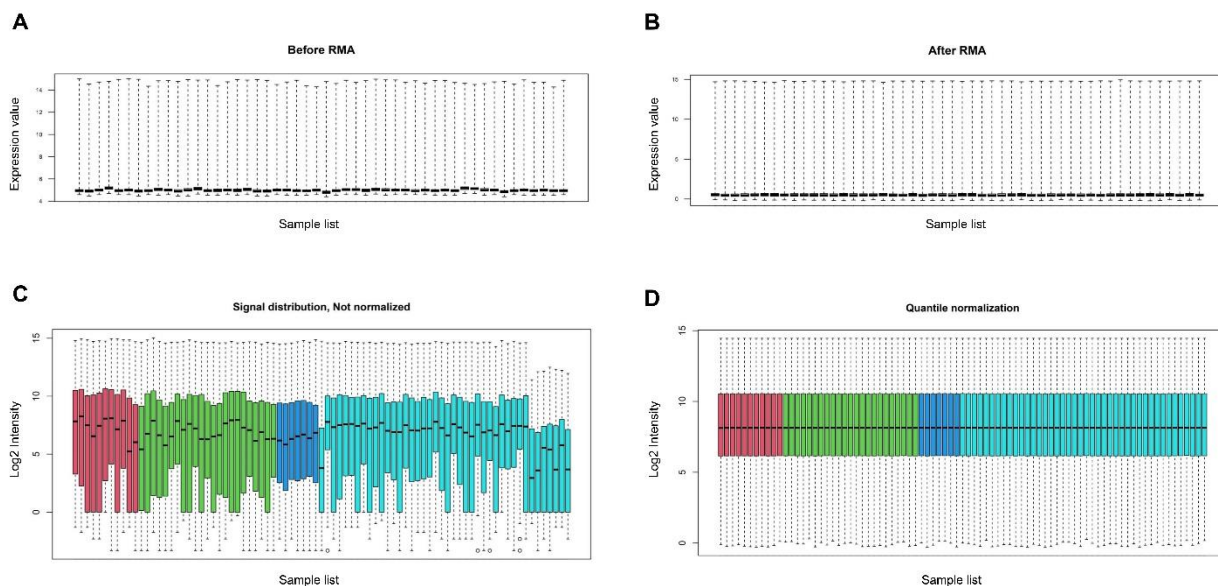
1 Supplementary Figures and Tables

1.1 Supplementary Figures

Supplementary Figure 1. The age distribution and sex distribution of 248 samples.



Supplementary Figure 2. Normalization of gene expression. (A-B) Normalization of the E-MTAB-1231 dataset. **(C-D)** Normalization of the E-MTAB-3303 dataset. Boxplots on the left represent data before normalization, and ones on the right represent data after normalization.



1.2 Supplementary Tables

Supplementary Table 1. Details of the ArrayExpress and GEO datasets.

EBI/GEO	Tissue (N)	Age-related miRNAs	Up	Down	Age	Reference
E-MTAB-3303	PBMC (83)	55	40	15	17-69	Xi Wang et al. (2015)
E-MTAB-1231	Mononuclear (50)	117	117	0	24-104	Serna E et al. (2013)
GSE89042	Leucocytes (38)	40	30	10	24-79	Muñoz-Culla M et al. (2017)

Supplementary Table 2. Primers used in our study.

Targets	Primers (5' to 3')
U6	Provided by TaKaRa Bio Inc
hsa-miR-107	F: CAGCAGCATTGTACAGGGCTATCA
hsa-miR-339-5p	F: TCCCTGTCCTCCAGGAGCT
hsa-miR-940	F: TATATAAGGCAGGGCCCCCG
hsa-miR-423-3p	F: TAGCTCGGTCTGAGGCCC
hsa-miR-27a-3p	F: CCTTCACAGTGGCTAAGTTCCGC
hsa-miR-652-3p	F: TAATGGCGCCACTAGGGTTGTG
hsa-miR-199a-5p	F: GCCCAGTGTTTCAGACTACCTGTTC
hsa-miR-222-3p	F: CCAGCTACATCTGGCTACTGGG
hsa-miR-1281	F: TTCGCCTCCTCCTCTCCC
hsa-miR-425-3p	Designed and synthesized by RiboBio
hsa-miR-1228-3p	F: TATATATCACACCTGCCTCGCCCC
hsa-miR-378a-3p	F: ACTGGACTTGGAGTCAGAAGGC
hsa-miR-330-3p	Designed and synthesized by RiboBio
hsa-miR-345-5p	F: GCTGACTCCTAGTCCAGGGC
hsa-miR-93-3p	F: ACTGCTGAGCTAGCACTTCCC

hsa-miR-491-5p	F: ATAGTGGGGAACCCTTCCATGAGG
hsa-miR-500a-3p	F: TATGCACCTGGGCAAGGATTCTG
hsa-miR-744-5p	F: TGCGGGGCTAGGGCTAA
18S rRNA	F: CTTGCTGGTCTGATTGTCGTT R: CTCGTCTGTTAGGTGGATGCT
hsa_circ_0007099	F: CTGCTGTGCTGTACGTGATC R: AGAGTTGTACAGTTGGGCCG
hsa_circ_0104147	F: GTGGTTCATGGGCTTTTGA R: TTAGGTCCAGCAGCACAGAA
hsa_circ_0005400	F: CCACCAACATTCTGACAGCA R: CAAAGTTCTGAAGCTGTGCCT
hsa_circ_0130015	F: GGAACCAGAAAAGATACGAGGC R: TCAGTGCGGTAGTCTTTTCTT
CircMYH11	F: TGCCTCCCAGATTCAAGTGA R: AAGAGTGACATCAGCAGCCT
CircNFATC3	F: AATATGTCAGCCAGCTCCTG R: CTGGTAAAATGCATGAGGTCGT
CircPPP2R5A	F: CCCAGAGAACGTGACTTCCT R: TCGTTTTGCAATGCTAGGCT
CircCAMLG	Failed in primer design
CircNCOA5	Failed in primer design
Novel_circ_0113405	F: CAATGTGCCAGCTCCATCTT R: TTCCTTGTCTCTGGGCATTCT

CircCNTRL	Failed in primer design
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CircBMP2	Failed in primer design
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Supplementary Table 3. Expression patterns and locations on human chromosomes of age-related miRNAs.

miRNA	Expression	Location on human chromosome
hsa-mir-107	Up	chr10: 89592747-89592827 [-]
hsa-mir-339	Up	chr7: 1022933-1023026 [-]
hsa-mir-146a	Controversial	chr5: 160485352-160485450 [+]
hsa-mir-940	Up	chr16: 2271747-2271840 [+]
hsa-mir-423-5p	Controversial	chr17: 30117079-30117172 [+]
hsa-mir-423-3p	Up	chr17: 30117079-30117172 [+]
hsa-mir-27a	Up	chr19: 13836440-13836517 [-]
hsa-mir-652	Up	chrX: 110055329-110055426 [+]
hsa-mir-199a	Up	chr19: 10817426-10817496 [-]
hsa-mir-222	Up	chrX: 45747015-45747124 [-]
hsa-let-7a	Controversial	chr9: 94175957-94176036 [+]
hsa-mir-25	Controversial	chr7: 100093560-100093643 [-]
hsa-let-7i	Controversial	chr12: 62603686-62603769 [+]
hsa-let-7g	Controversial	chr3: 52268278-52268361 [-]
hsa-let-7c	Controversial	chr21: 16539828-16539911 [+]
hsa-mir-1281	Up	chr22: 41092513-41092566 [+]

hsa-mir-425	Up	chr3: 49020148-49020234 [-]
hsa-mir-1228	Up	chr12: 57194504-57194576 [+]
hsa-mir-378	Up	chr5: 149732825-149732890 [+]
hsa-mir-944	Controversial	chr3: 189829922-189830009 [+]
hsa-mir-330	Up	chr19: 45638994-45639087 [-]
hsa-mir-345	Up	chr14: 100307859-100307956 [+]
hsa-mir-93	Up	chr7: 100093768-100093847 [-]
hsa-mir-491	Up	chr9: 20716105-20716188 [+]
hsa-mir-500a	Up	chrX: 50008431-50008514 [+]
hsa-mir-744	Up	chr17: 12081899-12081996 [+]

Supplementary Table 4. GO analysis of age-related miRNAs' target genes (show top 10 terms).

Terms	Description	Count	P-adj Value
GO:0048872	homeostasis of number of cells	19	0.003081005
GO:0034101	erythrocyte homeostasis	13	0.003081005
GO:0002262	myeloid cell homeostasis	14	0.003182789
GO:0030218	erythrocyte differentiation	12	0.004388056
GO:0030099	myeloid cell differentiation	24	0.00592676
GO:0071214	cellular response to abiotic stimulus	20	0.012491776
GO:0104004	cellular response to environmental stimulus	20	0.012491776
GO:0032648	regulation of interferon-beta production	7	0.026544388
GO:0009314	response to radiation	23	0.028027942
GO:0032608	interferon-beta production	7	0.028027942

Supplementary Table 5. KEGG pathway analysis of age-related miRNAs' target genes (show top 10).

Pathway	ID	Count	P-adj Value
Cellular senescence	hsa04218	15	0.001624013
Non-small cell lung cancer	hsa05223	8	0.021617616
FOXO signaling pathway	hsa04068	11	0.021617616
Viral carcinogenesis	hsa05203	14	0.021617616
Pancreatic cancer	hsa05212	8	0.021617616
Proteoglycans in cancer	hsa05205	14	0.021617616
Sphingolipid signaling pathway	hsa04071	10	0.023282768
Cell cycle	hsa04110	10	0.024770907
Breast cancer	hsa05224	11	0.024770907
Human T-cell leukemia virus 1 infection	hsa05166	14	0.024770907