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: CAGCAGCATGTGACTACAGGCTATCA                           |
| hsa-miR-339-5p| F: TCCCTGTCCTCCAGGAGCT                                  |
| hsa-miR-940   | F: TATATAAGGAGCAGGCCCC                                  |
| hsa-miR-423-3p| F: TAGCTCGGTCTGAGGCC                                   |
| hsa-miR-27a-3p| F: CCTTCACAGTGCTAAGTCCG                                   |
| hsa-miR-652-3p| F: TAATGGCCACAGGGTTGT                                    |
| hsa-miR-199a-5p| F: GCCCAGTGGTTCAGACTACCTGGT                                 |
| hsa-miR-222-3p| F: CCAGCTACATCTGGCAGTTGGG                                |
| hsa-miR-1281  | F: TTCCGCTCTCCCTCC                                      |
| hsa-miR-425-3p| Designed and synthesized by RiboBio                     |
| hsa-miR-1228-3p| F: TATATACACCTGCCTCGCC                                  |
| hsa-miR-378a-3p| F: ACTGGACTTGGAGTCCGAAGGC                                |
| hsa-miR-330-3p| Designed and synthesized by RiboBio                     |
| hsa-miR-345-5p| F: GCTGACTCCTAGTCCAGGGC                                 |
| hsa-miR-93-3p  | F: ACTGCTGAGCTAGCCTTCCC                                  |
| Transcript ID          | Forward Primer                  | Reverse Primer                  |
|-----------------------|---------------------------------|---------------------------------|
| hsa-miR-491-5p        | F: ATAGTGGGGAACCCCTCCATGAGG     |                                 |
| hsa-miR-500a-3p       | F: TATGCACCTGGGCAAGGATTCTG      |                                 |
| hsa-miR-744-5p        | F: TGCAGGGCTAGGGCTAA            |                                 |
| 18S rRNA              | F: CTTGCTGGTGCTGATTTGCGTT       | R: CTCGTCTGTTAGTGATGGCT        |
| hsa_circ_0007099      | F: CTGCTGTGCTGTACGTGATC         | R: AGAGTTGTACAGTTGGCCG         |
| hsa_circ_0104147      | F: GTGGTTGATGGGCTTTTGGA         | R: TTAGGTCCAGCAGCACAGAA        |
| hsa_circ_0005400      | F: CCACCAACATTCTGACAGCA         | R: CAAAGTTCTGAAGCTGTGCC        |
| hsa_circ_0130015      | F: GGAACCAAAAAGATACGAGG         | R: TCAGTGCGGTAGTCTTTTCTT       |
| CircMYH11             | F: TGCCTCCCAGATTCAAGTGA         | R: AAGAGTGCACATCGACGCT          |
| CircNFATC3            | F: AATATGTCAGCCAGCTCCTG         | R: CTGGTAAAAATGCATGAGGTCG      |
| CircPPP2R5A           | F: CCCAGAGAACGTGACTTCCCT       | R: TCGTTTTGCAAATGCTAGG         |
| CircCAMLG             | Failed in primer design         |                                 |
| CircNCOA5             | Failed in primer design         |                                 |
| Novel_circ_0113405    | F: CAATGTGCCAGCTCCATCTT         | R: TTCCTTGTCTGGGCAATTCT        |
**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   | 0.0124911776  |
| 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     |