iScience, Volume 27

Supplemental information

Expression quantitative trait locus

mapping of extracellular microRNAs

in human plasma

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Figure S1. Distribution of plasma ex-miRNA expression in 4,440

Framingham Heart Study participants. A) The histogram illustrates the distribution of expressed ex-miRNAs across different numbers of samples. B) The histogram illustrates the distribution of expressed ex-miRNAs across different Ct value ranges. Expressed ex-miRNAs were defined as having Ct values ≤34. The counts of expressed miRNAs within each bin are labeled at the top of their respective bars.



Number of Samples

В





Figure S2. Distribution of *cis***-exQTLs.** A) The histogram illustrates the number of *cis*-exQTL SNPs per miRNA; B) The histogram illustrates the distribution of the number of miRNA per *cis*-exQTL SNP vs. the number of *cis*-exQTL SNP per miRNA.



Α



Figure S3. A heatmap of ex-miRNAs in chr14 sharing *cis***-exQTL variants.** The color gradient represents the similarity score between any two miRNAs (e.g., miRNA A and miRNA B), calculated as the ratio of overlapped *cis*-exQTLs to the union of cis-exQTLs of miRNA A and miRNA B. miR-625-3p is situated on chromosome 14q23, while the remaining 17 miRNAs are located on chromosome 14q32.



Figure S4. The T values of exQTLs in all participants compared to the Generation Third cohort from FHS. A) *cis*-exQTLs; B) *trans*-exQTLs. Each dot represents an exQTL with a significance threshold of *P*<1e-4, with red dots indicating exQTLs passing the Bonferroni correction threshold (*P*<5e-8 for *cis* and *P*<1.78e-10 for *trans*).

Α



В

Figure S5. *cis*-exQTL variants minor allele frequency vs. effect size. Minor allele frequency of sentinel *cis*-exQTL variants (X-axis) vs. effect size of variants on exmiRNAs.



Figure S6. Distribution of coexpressed ex-miRNAs with different number of mRNAs. The counts of coexpressed ex-miRNAs within each bin are labeled at the top of their respective bars. The histogram illustrates most of ex-miRNA (N=212) coexpressed with less than 200 mRNAs. And, a few (N=14) coexpressed with more than 1000 mRNAs.

