## LEGENDS FOR SUPPLEMENTAL FIGURES AND DATASETS

FIGURE S1. Differentially expressed mRNAs in females and males as a function of age. (a, b) Volcano plot showing beta coefficients of mRNAs expressed with age (per year) in females (a) or males (b). mRNAs showing significantly increased (red dots) or decreased (blue dots) levels with age (p < 0.05). Gray dots show mRNAs that did not change significantly with age (p > 0.05). (c, d) Bar graphs showing the number of differentially expressed mRNAs in females (c) or males (d) using the linear regression or spline model.

**FIGURE S2.** Additional transcription factors putatively driving the expression of subsets of differentially abundant mRNAs with advanced aging. (a, b) GSEA of IRF1 (a) or transcription factors in the HOX family (b), enriched with advanced aging based on the differentially expressed mRNAs detected by linear regression model. (c) GSEA of LEF1 enriched with advanced aging based on the differentially expressed mRNAs detected by spline regression model.

FIGURE S3. Differentially expressed linear lncRNAs in females and males and enriched RNAbinding proteins interacting with differentially expressed linear lncRNAs with age based on spline regression model. (a, b) Volcano plot showing beta coefficients of linear lncRNAs expressed with age (per year) in female (a) and male (b) participants. LncRNAs showing significantly increased (red dots) or decreased (blue dots) levels with age (p < 0.05). Gray dots show lncRNAs that did not change significantly with age (p > 0.05). (c, d) Bar graphs showing the number of differentially expressed linear lncRNAs in females (c) or males (d) using the linear regression or spline model. (e) RNA-binding proteins interacting with linear lncRNAs, identified as being enriched by LncSEA analysis.

FIGURE S4. Differentially expressed circular lncRNAs in females and males with age. (a, b) Volcano plot showing beta coefficients of circular lncRNAs expressed with age (per year) in females (a) or males (b). Transcripts showing significantly increased (red dots) or decreased (blue dots) circular lncRNAs with age (p < 0.05). Gray dots indicate circular lncRNAs that did not change significantly with age (p > 0.05).

**SUPPLEMENTARY FILE S1. Coding RNAs.** Differentially expressed mRNAs using the linear and spline regression models. To take into consideration age-related trajectories, data were also analyzed separately for female and male participants.

**SUPPLEMENTARY FILE S2.** Overlap of mRNAs and proteins. Data used for establishing the correlations of the transcriptomic and proteomic analyses of the cohort.

**SUPPLEMENTARY FILE S3. Enriched TFs differentially abundant mRNAs.** Using the differentially expressed mRNAs, we performed GSEA to identify transcription factors which may regulate the expression of these prominent mRNAs.

**SUPPLEMENTARY FILE S4. mRNAs putative targets of FOX and HOX.** Differentially expressed mRNAs that were putative targets of forkhead box (FOX) and homeobox (HOX) transcription factors. Members of these two families were preferentially enriched based on GSEA reported in SUPPLEMENTARY FILE S3.

**SUPPLEMENTARY FILE S5. Linear lncRNAs.** Differentially expressed linear lncRNAs using the linear and spline regression models. To take into consideration age-related trajectories, data were also analyzed separately for female and male participants.

**SUPPLEMENTARY FILE S6. Enriched TFs for differentially abundant linear lncRNAs.** Using the differentially expressed linear lncRNAs, we used the LncSEA platform to identify transcription factors which may regulate the expression of these prominent linear lncRNAs.

**SUPPLEMENTARY FILE S7. Enriched RBPs for linear lncRNAs.** Using the differentially expressed linear lncRNAs, we used the LncSEA platform to identify RNA-binding proteins which may interact with these prominent linear lncRNAs.

**SUPPLEMENTARY FILE S8. circular lncRNAs.** Differentially expressed circular lncRNAs using the linear regression model. To take into consideration age-related trajectories, data were also analyzed separately for female and male participants.

**SUPPLEMENTARY FILE S9. Primer pairs.** Primer pairs employed in this study to validate the expression of lncRNAs (linear and circular) by using RT-qPCR analysis.





(d) 5 Number of differentially expressed mRNAs in male donors 0 1 0 0 0 0 0 0 0 0 3 -Spline model Linear

model

























