### Supplementary Table 1. PCR primers.

| Assay      | Component                        | Sequence                                      |
|------------|----------------------------------|-----------------------------------------------|
| mtDNA      | mtDNA Forward Primer (mtF805)    | 5′ CCACGGGAAACAGCAGTGATT 3′                   |
| mtDNA      | mtDNA Reverse Primer (mtR927)    | 5′ CTATTTGACTTGGGTAAATCGTGTGA 3′              |
| mtDNA      | mtDNA TaqMan Probe (LifeTechnologies) | 6FAM- 5′ TGCCAGCCACCGCG 3′-MGB             |
| Telomere Length | Telc              | 5′-TGT TAG GTA TCC CTA TCC CTA TCC CTA TCC CTA CTA ACA-3′ |
| Telomere Length | Telg          | 5′-ACA CTA AGG TTT GGG TTT GGG TTT GGG TTT GGG TTA GTG T-3′ |
| Telomere Length | Albd         | 5′-GCC CGG CCC GCC GCC CCC GTG GCC CGG AAAG AAAG CAC GTG TT-3′ |
| Telomere Length | Albu         | 5′-CGG CGG CGG CGG CGG GCT GG GCG AAA TGC TGC ACA GAA TCC TTG-3′ |

### Supplementary Table 2. Cross-sectional analysis of mitochondrial DNA copy number (mtDNAcn) and aging biomarkers.

| mtDNAcn * | DNAm-Age | DNAm-PhenoAge | DNAm-GrimAge | Telomere Length |
|-----------|----------|---------------|--------------|-----------------|
|           | β (95% CI) | P-value       | β (95% CI) | P-value | β (95% CI) | P-value | β (95% CI) | P-value |
| Q1        | Reference | 0.52          | Reference   | 0.02     | Reference | 0.91     | Reference | 0.06     |
|           | (-0.85, 0.43) | 0.52 | (-1.49, -0.12) | 0.02   | (-0.31, 0.28) | 0.91 | (-0.02, 0.13) | 0.13 |
| Q2        | -0.21     | 0.52          | -0.80       | 0.02     | -0.02     | 0.91     | -0.02     | 0.03     |
|           | (-1.29, 0.12) | 0.10 | (-1.75, -0.26) | 0.01   | (-0.35, 0.3) | 0.90 | (-0.05, 0.1) | 0.49 |
| Q3        | -1.11     | 0.10          | -0.83       | 0.04     | 0         | 1.00     | 0         | 0.04     |
|           | (-1.88, -0.35) | 0.01 | (-1.65, -0.02) | 0.04   | (-0.36, 0.36) | 1.00 | (-0.08, 0.06) | 0.80 |
| Q4        | -1.47     | 0.03          | -0.16       | 0.82     | 0.12      | 0.70     | 0.12      | 0.88     |
|           | (-2.79, -0.16) | 0.03 | (-1.48, 1.16) | 0.82   | (-0.47, 0.7) | 0.70 | (-0.11, 0.1) | 0.88 |
| p-trend** | -0.22     | 0.03          | -0.22       | 0.10     | -0.22     | 0.05     | -0.22     | 0.05     |

*All models adjusted for chronological age, smoking, alcohol use, BMI, cell composition, follow up time, hypertension status, CHD status, and diabetes status.

### Supplementary Table 3. Prospective analyses of baseline mitochondrial copy number (mtDNAcn) with aging biomarkers during follow up.

| mtDNAcn | DNAm-Age | DNAm-PhenoAge | DNAm-GrimAge | Telomere Length |
|---------|----------|---------------|--------------|-----------------|
|         | β (95% CI) | P-value       | β (95% CI) | P-value | β (95% CI) | P-value | β (95% CI) | P-value |
| Q1      | Reference | 0.45          | Reference   | 0.04     | Reference | 0.94     | Reference | 0.06     |
|         | (-1.35, 0.6) | 0.45 | (0.05, 2.04) | 0.04   | (-0.48, 0.45) | 0.94 | (-0.15, 0.02) | 0.16 |
| Q2      | -0.38     | 0.45          | 1.05        | 0.04     | -0.02     | 0.94     | -0.06     | 0.09     |
|         | (-1.35, 0.6) | 0.45 | (0.05, 2.04) | 0.04   | (-0.48, 0.45) | 0.94 | (-0.15, 0.02) | 0.16 |
| Q3      | -0.22     | 0.67          | 0.77        | 0.13     | 0.15      | 0.52     | -0.18     | 0.03     |
|         | (-1.2, 0.77) | 0.67 | (-0.23, 1.76) | 0.13   | (-0.31, 0.61) | 0.52 | (-0.18, -0.01) | 0.03 |
| Q4      | -0.23     | 0.64          | 1.38        | 0.01     | -0.02     | 0.93     | -0.17     | 0.06     |
|         | (-1.2, 0.74) | 0.64 | (0.38, 2.38) | 0.01   | (-0.48, 0.44) | 0.93 | (-0.17, 0) | 0.06 |
| p-trend** | -0.86    | 0.33          | 1.51        | 0.10     | -0.22     | 0.75     | -0.22     | 0.05     |
|         | (-2.6, 0.87) | 0.33 | (-0.29, 3.31) | 0.10   | (-1.64, 1.18) | 0.75 | (-0.31, 0) | 0.05 |

*All models adjusted for chronological age and outcome measure at baseline, follow up time, smoking, alcohol use, BMI, cell composition, hypertension status, CHD status, and diabetes status. **Using mtDNAcn as continuous models.