**Supplementary Tables**

**Supplementary file 4a. Sex differences in epigenetic aging after correction for body weight**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Predictor** | **Outcome** | **Estimate** | **Std Error** | **t Ratio** | **p** |
| Sex[M]lm(x ~ sex + BWF)n = 58(40 females, 18 males) | EAA, pan | 0.171 | 0.066 | 2.61 | 0.012 |
| EAA, liver | 0.098 | 0.055 | 1.79 | 0.079 |
| dev.EAA, pan | 0.180 | 0.059 | 3.05 | 0.004 |
| dev.EAA, liver | 0.176 | 0.057 | 3.07 | 0.003 |
| int.EAA, pan | 0.324 | 0.077 | 4.20 | 9.9E-05 |
| int.EAA, liver | 0.133 | 0.078 | 1.72 | 0.092 |

**Supplementary file 4b. Pearson correlations between epigenetic age acceleration and strain-level longevity summaries**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **DNAm** | **minLS** | **25Q-LS** | **Mean LS** | **Median LS** | **75Q-LS** | **Max LS** |
| **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** |
| EAA, pan | 0.08 | 0.15 | 0.06 | 0.27 | -0.06 | 0.34 | -0.08 | 0.17 | -0.16 | 0.005 | -0.13 | 0.02 |
| EAA, liver | -0.02 | 0.73 | -0.03 | 0.58 | -0.07 | 0.24 | -0.08 | 0.18 | -0.08 | 0.15 | -0.06 | 0.27 |
| dev.EAA, pan | -0.02 | 0.70 | 0.03 | 0.59 | -0.02 | 0.69 | -0.04 | 0.50 | -0.06 | 0.33 | -0.01 | 0.91 |
| dev.EAA, liver | -0.05 | 0.35 | -0.01 | 0.83 | -0.05 | 0.37 | -0.08 | 0.18 | -0.07 | 0.21 | 0.01 | 0.86 |
| int.EAA, pan | 0.02 | 0.73 | -0.01 | 0.91 | -0.05 | 0.35 | -0.09 | 0.12 | -0.08 | 0.17 | -0.04 | 0.48 |
| int.EAA, liver | -0.19 | 0.0007 | -0.15 | 0.01 | -0.19 | 0.001 | -0.19 | 0.001 | -0.18 | 0.002 | -0.14 | 0.02 |

n = 302 females BXDs belonging to 65 genotype-by-diet combinations with at least n = 5 observations of age at natural death.

38 BXD genotypes on normal chow, and 27 BXD genotypes on high fat diet.

**Supplementary file 4c. High priority candidate genes in QTLs for epigenetic age acceleration**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | **Missense/stop variant in the BXD** |  | **Human GWAS**  |
| **Gene** | **Chr** | **Mb** | **Csq a** | **dbSNP a** | **Ref a** | ***D* a** | **LOD (high allele)b** | **Human trait** | **Reference** |
| *Mmd* | 11 | 90.25 | cis-eQT |  |  |  | 7.4 (B) | Menarche (age at onset) | 1 |
| *Stxbp4* | 11 | 90.54 | missense; cis-eQT | rs3668623 | C | T | 6.1 (D) | Intrinsic epigenetic age acceleration; Menarche (age at onset) | 2-4 |
| *Tom1l1* | 11 | 90.67 | missense; cis-eQT | rs13469307; rs13469308 | G; G | A; C | 2.7 (D) | Parental longevity (mother's age at death or mother's attained age) | 5 |
| *Abi3* | 11 | 95.83 | missense | rs29392269 | G | A |  | Late onset & and family history of Alzheimer's disease | 6,7  |
| *Cdk12* | 11 | 98.20 | missense | rs27086373 | C | A |  | Menopause (age at onset) | 8 |
| *Cyp26a1* | 19 | 37.70 | missense | rs8236989 | G | A |  | Human longevity | 9 |
| *Myof* | 19 | 38.00 | missense | rs31052565; rs46477910 | A; G | G; T |  | Human longevity | 9 |
| *Ccnj* | 19 | 40.83 | missense; cis-eQT | rs36487301 | C | A | 4.1 (D) | Menopause (age at onset) | 10 |
| *Nkx2-3* | 19 | 43.62 | missense | rs30898786 | T | G |  | Epigenetic age acceleration (PhenoAge) | 11 |
| *Cutc* | 19 | 43.75 | cis-eQT |  |  |  | 37.6 (B) | Epigenetic age acceleration (Hannum and PhenoAge) | 11 |
| *Chuk* | 19 | 44.08 | missense | rs48727905 | T | G |  | Age at menopause | 1 |
| *Pkd2l1* | 19 | 44.15 | missense | rs30956598; rs13483639 | A; T | G; C |  | Parental extreme longevity (95 years and older) | 12 |

**a** Data from the Wellcome Sanger Institute Mouse Genome Project. Each gene also contains multiple non-coding variants. Ref (reference) is the allele for C57BL/6J; *D* is the allele for DBA/2J.

**b** LOD score for gene expression *cis*-eQTL in BXD liver. *B* means the C57BL/6J allele has the positive additive effect; *D* means the DBA/2J allele has the positive additive effect.

**Reference for Supplementary file 4c:**

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