

## Supplementary Methods

### Skin aging phenotyping methods

Multiple phenotypes were generated in the project. Photonumerical classification and semi-automated computational quantitative methods were used to define facial skin aging phenotypes. For all participants, 2D facial images (three angles including full face, right, and left profiles) and high-resolution 3D facial scans were obtained under optimized conditions with a standardized viewpoint, appropriate lighting, without makeup or jewelry using the VECTRA® H1 imaging system (Canfield Scientific, Inc.). Preprocessing of 3D scans and conversion of 3D to 2D photographs was performed using VECTRA® H1 software version 6.2. Semi-automated facial wrinkle detection and quantification were done using MATLAB software (MATLAB. (2018). 9.7.0.1190202 (R2019b). Natick, Massachusetts: The MathWorks Inc.). The grayscale images were preprocessed and smoothed by applying the Gaussian filter [1] and masked to isolate the face skin area of interest, excluding eyes, eyebrows, nose, and mouth areas. Wrinkles were detected using the Canny Edge Detector algorithm [2]. The detected wrinkles were quantified by calculating facial wrinkle area (pixels detected as wrinkles as a percentage of the total skin area) and wrinkle length (length of areas detected as wrinkles normalized by the square root of the total skin area) [3].

Assessment of other facial aging traits was also conducted either by a board-certified dermatologist or by the participants themselves, and included the following: i) **perceived facial age** estimation, determined by visual assessment of the participant's facial appearance without prior knowledge of chronological age [4]; perceived age was assessed by a professional dermatologist involved in the project, who performed the evaluation based on 3D facial scans and 2D photographs; in the first stage, following an initial analysis, the dermatologist estimated the age within a  $\pm 5$ -year range; during the second assessment, a more precise perceived age was assigned based on the person's facial appearance; ii) **subjective aging rate**, determined by the participants themselves based on how old they felt (0 - younger than real age, 1 - same as real

age, 2 - older than real age); iii) **the Glogau classification of photoaging** to categorize skin types from I to IV, indicating respectively: no wrinkles, wrinkles in motion, wrinkles at rest, and wrinkles only [5]; iv) the photonumeric/binary score of facial skin aging to assess **the presence of wrinkles** in different areas of the face, including the full face, forehead, eye area (crow's feet wrinkles), and lip wrinkles. Measurements were classified as either deep or small. The presence of eyelid drooping, nasolabial folds, pigmentation spots, telangiectasia, facial height and lip height were also recorded. Additionally, the spectrophotometric measurement of skin color using the Fitzpatrick skin typing scale was determined (**Supplementary Table 3**).

### **DNA methylation quantification**

DNA from blood for all samples collected in the study (N=735) was extracted using an automated method and the Maxwell RSC Blood DNA Kit (Promega Corporation), followed by determination of purity using NanoDrop (Thermo Scientific, MA, USA) and concentration using the Qubit dsDNA HS Assay Kit (Thermo Fisher Scientific). The amount of 500 ng DNA per sample was subjected to bisulfite conversion using the EZ-96 DNA Methylation Kit (Zymo Research Corp., CA, USA) according to the manufacturer's instructions for Infinium assays. DNA samples were randomized using the web-based application RANDOMIZE [6], and the methylation profile for all samples was obtained using the Illumina Infinium Methylation EPIC microarray (Illumina, San Diego, CA, USA). Primary quality control of the generated DNA methylation data was performed using the GenomeStudio software and the Methylation Module v1.8 (Illumina Inc, 2008) [7]. Further sample and probe-based quality control was performed in R version 4.2 using the minfi [8] and limma [9] R packages. A p-value threshold of 0.05 and 0.01 was used for probe and sample call rates, respectively. Two types of normalization, quantile normalization, were applied for the downstream epigenetic age estimation and epigenome-wide association (EWAS) analyses, respectively. The methylation level was

calculated as the  $\beta$  value (the ratio of the methylated signal to the total signal per probe, with an added constant in the denominator ranging from 0 and 1). In addition, for EWAS further probe filtering steps were performed to exclude the list of probes if they were I) mapped to X and Y chromosomes (except for hair loss), II) reported to overlap with SNPs, III) cross-reactive mapped to multiple genomic locations [10], IV) problematic probes reported by Illumina.

DMPs significantly associated (FDR  $p < 0.05$ ) with specific phenotypes were identified through a series of EWAS analyses and using the limma package [9]. Linear models were fitted using derived methylation M-values, the log<sub>2</sub> ratio of the intensities obtained from methylated probes to unmethylated probes. In fitted model 1, the results of the EWAS analysis were adjusted for age, sex, and cell components. Model 2 was additionally adjusted for environmental factors.

### **Profiling of epigenetic clocks and associations with facial skin aging**

Epigenetic age was estimated for all samples studied using the methylCIPHER R package for several DNAm-based biomarkers, including DNAm age Horvath2013, DNAm age Hannum, DNAm age Skin&Blood, DNAm PhenoAge, DNAm GrimAge, and DNAm FitAge [11–17]. The methylation level, represented as the  $\beta$  value, was used as the input. The corresponding epigenetic age acceleration (EAA) measures were calculated as the residuals of regressing DNAm age on chronological age. EAA measures included the intrinsic epigenetic age acceleration (IEAA) calculated by regressing the Horvath2013 clock on chronological age, extrinsic epigenetic age acceleration (EEAA) estimated by regressing the Hannum clock on chronological age, DNAm PhenoAge acceleration (PhenoAgeAccel), DNAm GrimAge acceleration (GrimAgeAccel), DNAm FitAge acceleration (FitAgeAccel). In addition, DNAm-based pace of aging (PACE and PoAm) and epigenetic Mortality Risk Score (Zhang MRS) were measured [18–20]. The Steve Horvath & Clock Foundation online algorithm

(<https://dnamage.clockfoundation.org/>) was used to estimate the methylation-based blood cell components [11,21]. For missing CpGs included in different clocks, we followed the imputation procedure described in the Horvath online calculator. Specifically, k-nearest neighbor (kNN) imputation with  $k = 10$  was applied to fill in missing values within each clock. For CpGs missing across all samples (i.e., probes not covered by the Illumina EPIC v1 array), we used the Horvath “gold-standard” imputation approach, replacing missing values with the mean values provided in the datMiniAnnotation3 reference list. For calculating DunedinPACE, 173 probes were used, and any missing values were replaced with the cohort-specific mean, as described in the official DunedinPACE GitHub documentation [18]. A default threshold of 0.7 was applied.

The EAA measures were next tested for association with different skin and hair phenotypes. Model 1 was adjusted for sex and age, and model 2 was additionally adjusted for smoking status, stress level, skin color, frequency of tanning or solarium use, and blood cell proportions.

### **Genome-wide association analyses**

The Global Screening Array (GSA) from Illumina (San Diego, CA) was used for sample genotyping. Quality control prior to imputation was performed using PLINK1.9 [40]. Samples or SNPs with more than 5% missing data were excluded, and SNPs with significant deviation from Hardy-Weinberg equilibrium were filtered based on  $p < 1.0 \times 10^{-6}$ . The minor allele frequency (MAF) threshold was set at  $< 0.01$ . Only biallelic SNPs on autosomal chromosomes mapped to a unique genomic location were retained for further analysis. Principal component analysis (PCA) was performed on the pruned variants to detect population stratification or genetic outliers. SNPs were then imputed using Beagle version 5.4 [41]. The final number of 719 samples and 477,827 SNPs were used for genome-wide association analyses (GWAS).

performed using linear regression for testing genetic association with continuous skin aging phenotypes and logistic regression for binary skin aging traits under an additive genetic model. Multivariate regression models were adjusted for age, sex, BMI, skin color, smoking status, DNA methylation pack-years, stress level, solarium exposure, tanning frequency, and a p-value threshold of  $<5 \times 10^{-8}$  was considered statistically significant.

## References

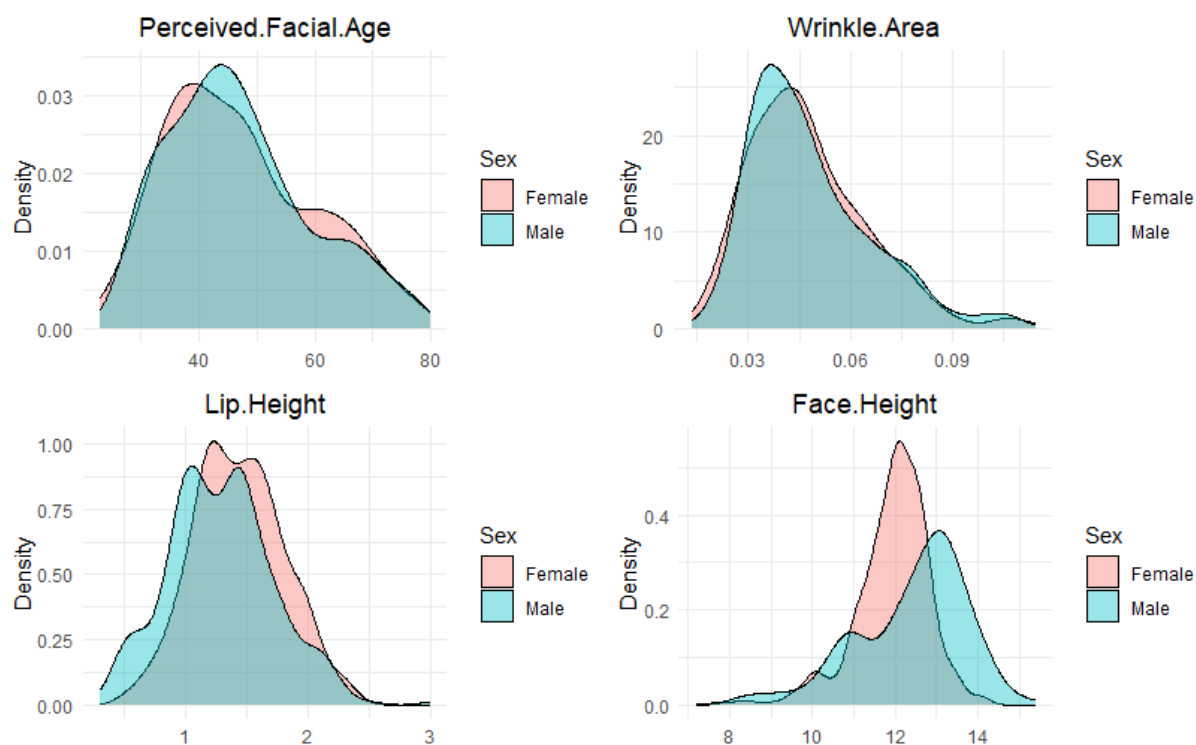
- [1] R. González, R. Woods, S.L. Eddins, Digital image processing using MATLAB, (2006).
- [2] Y.M. Luo, R. Duraiswami, Canny edge detection on NVIDIA CUDA, 2008 IEEE Computer Society Conference on Computer Vision and Pattern Recognition Workshops (2008). <https://doi.org/10.1109/CVPRW.2008.4563088>.
- [3] M.A. Hamer, L.C. Jacobs, J.S. Lall, A. Wollstein, L.M. Hollestein, A.R. Rae, K.W. Gossage, A. Hofman, F. Liu, M. Kayser, T. Nijsten, D.A. Gunn, Validation of image analysis techniques to measure skin aging features from facial photographs, *Skin Research and Technology* 21 (2015) 392–402. <https://doi.org/10.1111/SRT.12205>.
- [4] M. Coma, R. Valls, J.M. Mas, A. Pujol, M.A. Herranz, V. Alonso, J. Naval, Methods for diagnosing perceived age on the basis of an ensemble of phenotypic features, *Clin Cosmet Investig Dermatol* 7 (2014) 133–137. <https://doi.org/10.2147/CCID.S52257>.
- [5] R.G. Glogau, Aesthetic and anatomic analysis of the aging skin., *Semin Cutan Med Surg* 15 (1996) 134–138. [https://doi.org/10.1016/S1085-5629\(96\)80003-4](https://doi.org/10.1016/S1085-5629(96)80003-4).
- [6] A.H. Wani, J. Dahrendorff, M. Uddin, RANDOMIZE: A Web Server for Data Randomization, (n.d.). <https://doi.org/10.1101/2020.04.02.013656>.
- [7] Illumina, GenomeStudio Methylation Module v1.8 User Guide (11319130), (2010).
- [8] J.P. Fortin, T.J. Triche, K.D. Hansen, Preprocessing, normalization and integration of the Illumina HumanMethylationEPIC array with minfi, *Bioinformatics* 33 (2017) 558. <https://doi.org/10.1093/BIOINFORMATICS/BTW691>.
- [9] M.E. Ritchie, B. Phipson, D. Wu, Y. Hu, C.W. Law, W. Shi, G.K. Smyth, limma powers differential expression analyses for RNA-sequencing and microarray studies, *Nucleic Acids Res* 43 (2015) e47. <https://doi.org/10.1093/NAR/GKV007>.
- [10] Y.-A. Chen, M. Lemire, S. Choufani, D.T. Butcher, D. Grafodatskaya, B.W. Zanke, S. Gallinger, T.J. Hudson, R. Weksberg, Discovery of cross-reactive probes and polymorphic CpGs in the Illumina Infinium HumanMethylation450 microarray, *Epigenetics* 203 *Epigenetics* 8 (2013) 203–209. <https://doi.org/10.4161/epi.23470>.
- [11] S. Horvath, DNA methylation age of human tissues and cell types, *Genome Biol* 14 (2013). <https://doi.org/10.1186/gb-2013-14-10-r115>.

- [12] A.T. Lu, A. Quach, J.G. Wilson, A.P. Reiner, A. Aviv, K. Raj, L. Hou, A.A. Baccarelli, Y. Li, J.D. Stewart, E.A. Whitsel, T.L. Assimes, L. Ferrucci, S. Horvath, DNA methylation GrimAge strongly predicts lifespan and healthspan, *Aging (Albany NY)* 11 (2019) 303. <https://doi.org/10.18632/AGING.101684>.
- [13] M.E. Levine, A.T. Lu, A. Quach, B.H. Chen, T.L. Assimes, S. Bandinelli, L. Hou, A.A. Baccarelli, J.D. Stewart, Y. Li, E.A. Whitsel, J.G. Wilson, A.P. Reiner<sup>1</sup>, A. Aviv<sup>1</sup>, K. Lohman, Y. Liu, L. Ferrucci, S. Horvath, An epigenetic biomarker of aging for lifespan and healthspan, *Aging* 10 (2018) 573–591. <https://doi.org/10.18632/AGING.101414>.
- [14] K.M. McGreevy, Z. Radak, F. Torma, M. Jokai, A.T. Lu, D.W. Belsky, A. Binder, R.E. Marioni, L. Ferrucci, E. Pośpiech, W. Branicki, A. Ossowski, A. Sitek, M. Spólnicka, L.M. Raffield, A.P. Reiner, S. Cox, M. Kobor, D.L. Corcoran, S. Horvath, DNAmFitAge: biological age indicator incorporating physical fitness, *Aging* 15 (2023). <https://doi.org/10.18632/AGING.204538>.
- [15] S. Horvath, J. Oshima, G.M. Martin, A.T. Lu, A. Quach, H. Cohen, S. Felton, M. Matsuyama, D. Lowe, S. Kabacik, J.G. Wilson, A.P. Reiner, A. Maierhofer, J. Flunkert, A. Aviv, L. Hou, A.A. Baccarelli, Y. Li, J.D. Stewart, E.A. Whitsel, L. Ferrucci, S. Matsuyama, K. Raj, Epigenetic clock for skin and blood cells applied to Hutchinson Gilford Progeria Syndrome and ex vivo studies, *Aging* 10 (2018) 1758–1775. <https://doi.org/10.18632/AGING.101508>.
- [16] G. Hannum, J. Guinney, L. Zhao, L. Zhang, G. Hughes, S.V. Sadda, B. Klotzle, M. Bibikova, J.B. Fan, Y. Gao, R. Deconde, M. Chen, I. Rajapakse, S. Friend, T. Ideker, K. Zhang, Genome-wide Methylation Profiles Reveal Quantitative Views of Human Aging Rates, *Mol Cell* 49 (2013) 359–367. <https://doi.org/10.1016/j.molcel.2012.10.016>.
- [17] A.T. Lu, A. Seeboth, P.C. Tsai, D. Sun, A. Quach, A.P. Reiner, C. Kooperberg, L. Ferrucci, L. Hou, A.A. Baccarelli, Y. Li, S.E. Harris, J. Corley, A. Taylor, I.J. Deary, J.D. Stewart, E.A. Whitsel, T.L. Assimes, W. Chen, S. Li, M. Mangino, J.T. Bell, J.G. Wilson, A. Aviv, R.E. Marioni, K. Raj, S. Horvath, DNA methylation-based estimator of telomere length, *Aging* 11 (2019) 5895–5923. <https://doi.org/10.18632/AGING.102173>.
- [18] D.W. Belsky, A. Caspi, D.L. Corcoran, K. Sugden, R. Poulton, L. Arseneault, A. Baccarelli, K. Chamarti, X. Gao, E. Hannon, H.L. Harrington, R. Houts, M. Kothari, D. Kwon, J. Mill, J. Schwartz, P. Vokonas, C. Wang, B. Williams, T.E. Moffitt, DunedinPACE, a DNA methylation biomarker of the pace of aging, *Elife* 11 (2022). <https://doi.org/10.7554/ELIFE.73420>.
- [19] D.W. Belsky, A. Caspi, L. Arseneault, A. Baccarelli, D. Corcoran, X. Gao, E. Hannon, H.L. Harrington, L.J.H. Rasmussen, R. Houts, K. Huffman, W.E. Kraus, D. Kwon, J. Mill, C.F. Pieper, J. Prinz, R. Poulton, J. Schwartz, K. Sugden, P. Vokonas, B.S. Williams, T.E. Moffitt, Quantification of the pace of biological aging in humans through a blood test, the DunedinPoAm DNA methylation algorithm, *Elife* 9 (2020) 1–56. <https://doi.org/10.7554/ELIFE.54870>.
- [20] Y. Zhang, R. Wilson, J. Heiss, L.P. Breitling, K.U. Saum, B. Schöttker, B. Holleczer, M. Waldenberger, A. Peters, H. Brenner, DNA methylation signatures in peripheral blood strongly predict all-cause mortality, *Nat Commun* 8 (2017). <https://doi.org/10.1038/NCOMMS14617>.
- [21] E.A. Houseman, W.P. Accomando, D.C. Koestler, B.C. Christensen, C.J. Marsit, H.H. Nelson, J.K. Wiencke, K.T. Kelsey, DNA methylation arrays as surrogate measures of cell mixture distribution, *BMC Bioinformatics* 13 (2012) 86. <https://doi.org/10.1186/1471-2105-13-86>.

## Supplementary Figures



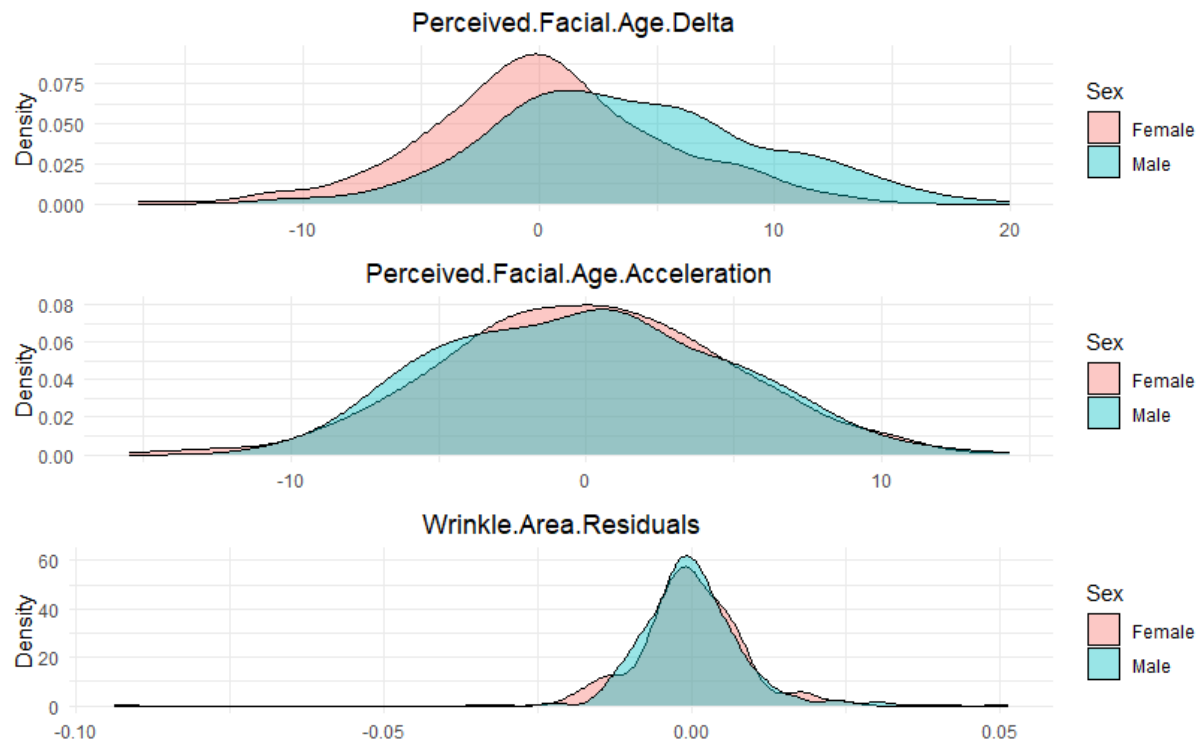
**Supplementary Figure 1.** Age profile of the studied population (N=735): histogram. Mean  $\pm$  SD: 46.4  $\pm$  14.7 years; Median: 45 years.



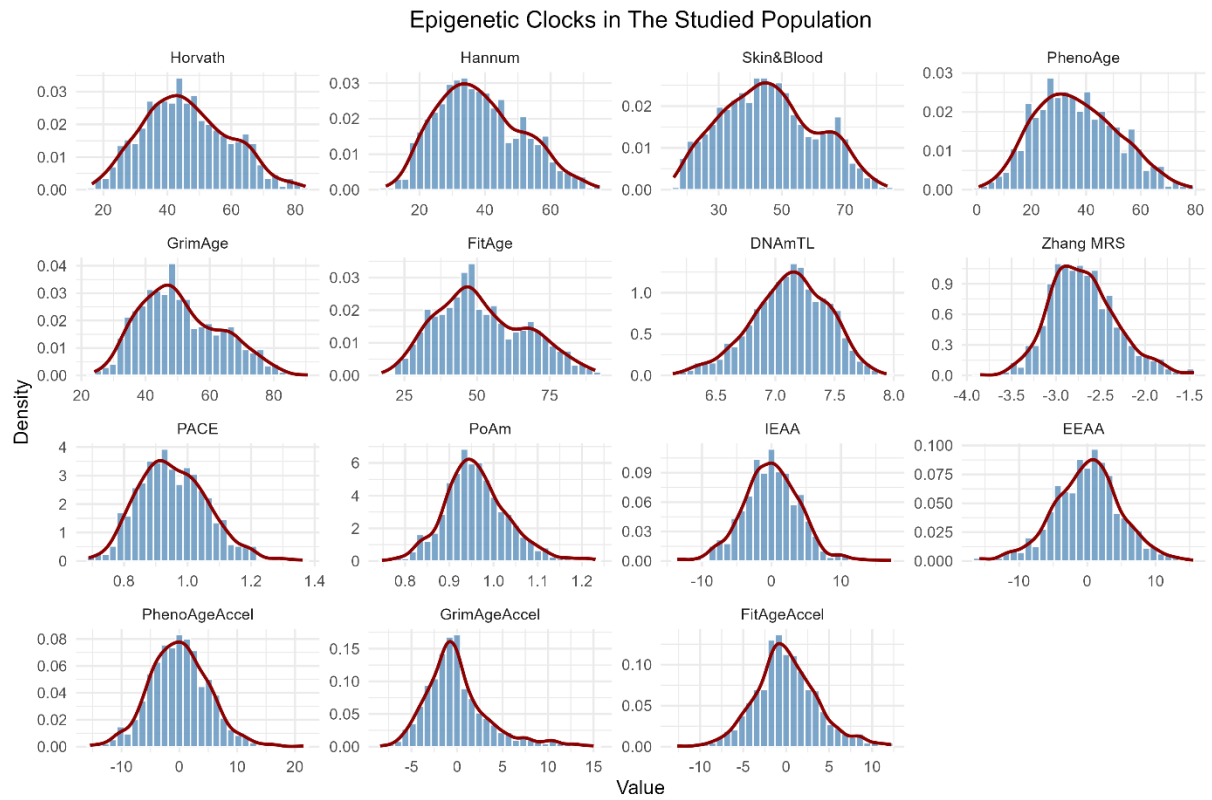
**Supplementary Figure 2.** Density plots of quantitative skin-aging phenotypes analysed in the study.



**Supplementary Figure 3.** Bar plots for categorical skin aging phenotypes analysed in the study.



**Supplementary Figure 4.** Adjusted skin aging phenotype distribution. To remove the effects of confounding factors for the purposes of predictive analysis, instead of using absolute values the phenotypes wrinkle area and perceived facial age were adjusted for the effects of age and/or sex. The parameter perceived facial age delta represents the simple difference between perceived age and chronological age. The parameters perceived facial age acceleration and wrinkle area residuals are calculated as the residuals from regression of perceived facial age and wrinkle area on both chronological age and sex.



**Supplementary Figure 5.** Epigenetic clock profiles across the study population (N=735): histogram representation.

## Supplementary Tables

Supplementary Tables 5, 6, 7, 8, 10, 13, 14, 15, 16, 17, and 18 are provided in a separate Excel file.

**Supplementary Table 1.** Demographic information of study participants.

|                                        | Female (N=379) | Male (N=356) | All subjects (N=735) |
|----------------------------------------|----------------|--------------|----------------------|
| <b>Age</b>                             |                |              |                      |
| Mean (SD)                              | 47.8 (13.7)    | 45.0 (15.6)  | 46.4 (14.7)          |
| <b>Education</b>                       |                |              |                      |
| University                             | 256 (67.5%)    | 225 (63.2%)  | 481 (65.4%)          |
| No University                          | 123 (32.5%)    | 130 (36.5%)  | 253 (34.4%)          |
| Missing                                | 0 (0%)         | 1 (0.3%)     | 1 (0.1%)             |
| <b>Socioeconomic status (SES)</b>      |                |              |                      |
| Low-SES                                | 21 (5.5%)      | 8 (2.2%)     | 29 (3.9%)            |
| Medium-SES                             | 284 (74.9%)    | 249 (69.9%)  | 533 (72.5%)          |
| High-SES                               | 72 (19.0%)     | 96 (27.0%)   | 168 (22.9%)          |
| Missing                                | 2 (0.5%)       | 3 (0.8%)     | 5 (0.7%)             |
| <b>Area of residence</b>               |                |              |                      |
| Village                                | 64 (16.9%)     | 59 (16.6%)   | 123 (16.7%)          |
| City<100K                              | 63 (16.6%)     | 59 (16.6%)   | 122 (16.6%)          |
| City>100K                              | 251 (66.2%)    | 236 (66.3%)  | 487 (66.3%)          |
| Missing                                | 1 (0.3%)       | 2 (0.6%)     | 3 (0.4%)             |
| <b>Type of job</b>                     |                |              |                      |
| Intern/retired/unemployed              | 70 (18.5%)     | 55 (15.4%)   | 125 (17.0%)          |
| Sedentary mental work (SM)             | 112 (29.6%)    | 86 (24.2%)   | 198 (26.9%)          |
| Long hours sedentary mental work (LSM) | 159 (42.0%)    | 120 (33.7%)  | 279 (38.0%)          |
| Manual (M)                             | 37 (9.8%)      | 93 (26.1%)   | 130 (17.7%)          |
| Missing                                | 1 (0.3%)       | 2 (0.6%)     | 3 (0.4%)             |

**Supplementary Table 2.** Participants' lifestyle information.

|                                          | <b>Female (N=379)</b> | <b>Male (N=356)</b> | <b>All subjects (N=735)</b> |
|------------------------------------------|-----------------------|---------------------|-----------------------------|
| <b>BMI</b>                               |                       |                     |                             |
| Mean (SD)                                | 25.5 (4.8)            | 27.6 (4.1)          | 26.5 (4.6)                  |
| Missing                                  | 3 (0.8%)              | 2 (0.6%)            | 5 (0.7%)                    |
| <b>Smoking status</b>                    |                       |                     |                             |
| Never smoker                             | 229 (60.4%)           | 177 (49.7%)         | 406 (55.2%)                 |
| Former smoker                            | 77 (20.3%)            | 77 (21.6%)          | 154 (21.0%)                 |
| Current smoker                           | 73 (19.3%)            | 99 (27.8%)          | 172 (23.4%)                 |
| Missing                                  | 0 (0%)                | 3 (0.8%)            | 3 (0.4%)                    |
| <b>Alcohol drinking</b>                  |                       |                     |                             |
| Never                                    | 52 (13.7%)            | 34 (9.6%)           | 86 (11.7%)                  |
| Occasionally                             | 295 (77.8%)           | 268 (75.3%)         | 563 (76.6%)                 |
| Frequently                               | 31 (8.2%)             | 51 (14.3%)          | 82 (11.2%)                  |
| Missing                                  | 1 (0.3%)              | 3 (0.8%)            | 4 (0.5%)                    |
| <b>Physical activity (PA)</b>            |                       |                     |                             |
| Inactive                                 | 92 (24.3%)            | 61 (17.1%)          | 153 (20.8%)                 |
| Active                                   | 287 (75.7%)           | 294 (82.6%)         | 581 (79.0%)                 |
| Missing                                  | 0 (0%)                | 1 (0.3%)            | 1 (0.1%)                    |
| <b>Self-report of stress sensitivity</b> |                       |                     |                             |
| FALSE                                    | 359 (94.7%)           | 274 (77.0%)         | 633 (86.1%)                 |
| TRUE                                     | 20 (5.3%)             | 82 (23.0%)          | 102 (13.9%)                 |
| <b>Yoga/meditation</b>                   |                       |                     |                             |
| FALSE                                    | 324 (85.5%)           | 343 (96.3%)         | 667 (90.7%)                 |
| TRUE                                     | 55 (14.5%)            | 13 (3.7%)           | 68 (9.3%)                   |
| <b>Sleeping hours</b>                    |                       |                     |                             |
| Mean (SD)                                | 6.7 (1.2)             | 6.7 (1.1)           | 6.7 (1.1)                   |
| Missing                                  | 0 (0%)                | 3 (0.8%)            | 3 (0.4%)                    |
| <b>Type of diet</b>                      |                       |                     |                             |
| Varied                                   | 357 (94.2%)           | 332 (93.3%)         | 689 (93.7%)                 |

|                             | <b>Female (N=379)</b> | <b>Male (N=356)</b> | <b>All subjects (N=735)</b> |
|-----------------------------|-----------------------|---------------------|-----------------------------|
| Protein                     | 4 (1.1%)              | 16 (4.5%)           | 20 (2.7%)                   |
| Vegetarian                  | 17 (4.5%)             | 6 (1.7%)            | 23 (3.1%)                   |
| Missing                     | 1 (0.3%)              | 2 (0.6%)            | 3 (0.4%)                    |
| <b>Sugar intake</b>         |                       |                     |                             |
| Low                         | 27 (7.1%)             | 31 (8.7%)           | 58 (7.9%)                   |
| Medium                      | 275 (72.6%)           | 274 (77.0%)         | 549 (74.7%)                 |
| High                        | 77 (20.3%)            | 50 (14.0%)          | 127 (17.3%)                 |
| Missing                     | 0 (0%)                | 1 (0.3%)            | 1 (0.1%)                    |
| <b>Frequency of tanning</b> |                       |                     |                             |
| Rarely                      | 207 (54.6%)           | 208 (58.4%)         | 415 (56.5%)                 |
| Frequently                  | 171 (45.1%)           | 144 (40.4%)         | 315 (42.9%)                 |
| Missing                     | 1 (0.3%)              | 4 (1.1%)            | 5 (0.7%)                    |
| <b>Solarium use</b>         |                       |                     |                             |
| Never                       | 222 (58.6%)           | 287 (80.6%)         | 509 (69.3%)                 |
| Former History              | 129 (34.0%)           | 54 (15.2%)          | 183 (24.9%)                 |
| Currently                   | 28 (7.4%)             | 14 (3.9%)           | 42 (5.7%)                   |
| Missing                     | 0 (0%)                | 1 (0.3%)            | 1 (0.1%)                    |
| <b>Cups of coffee</b>       |                       |                     |                             |
| None                        | 58 (15.3%)            | 79 (22.2%)          | 137 (18.6%)                 |
| Small (1-2/day)             | 245 (64.6%)           | 164 (46.1%)         | 409 (55.6%)                 |
| Large ( $\geq 3$ /day)      | 69 (18.2%)            | 109 (30.6%)         | 178 (24.2%)                 |
| Missing                     | 7 (1.8%)              | 4 (1.1%)            | 11 (1.5%)                   |

**Supplementary Table 3.** Facial skin aging characteristics of the study participants.

|                                             |  | Female (N=379)            |  | Male (N=356)              |  | All subjects (N=735)      |
|---------------------------------------------|--|---------------------------|--|---------------------------|--|---------------------------|
| <b>Perceived facial age</b>                 |  |                           |  |                           |  |                           |
| Mean (SD)                                   |  | 47.1 (12.8)               |  | 46.9 (12.3)               |  | 47.0 (12.5)               |
| Median (Q1, Q3)                             |  | 45.0 (37.3, 56.0)         |  | 45.0 (38.0, 55.0)         |  | 45.0 (38.0, 55.0)         |
| Missing                                     |  | 53 (14.0%)                |  | 33 (9.3%)                 |  | 86 (11.7%)                |
| <b>Subjective aging rate</b>                |  |                           |  |                           |  |                           |
| 0 (Younger than real age)                   |  | 165 (43.5%)               |  | 130 (36.5%)               |  | 295 (40.1%)               |
| 1 (As real age)                             |  | 179 (47.2%)               |  | 186 (52.2%)               |  | 365 (49.7%)               |
| 2 (Older than real age)                     |  | 30 (7.9%)                 |  | 38 (10.7%)                |  | 68 (9.3%)                 |
| Missing                                     |  | 5 (1.3%)                  |  | 2 (0.6%)                  |  | 7 (1.0%)                  |
| <b>Wrinkle area %</b>                       |  |                           |  |                           |  |                           |
| Mean (SD)                                   |  | 4.8 (1.8)                 |  | 4.8 (1.8)                 |  | 4.8 (1.8)                 |
| Median (Q1, Q3)                             |  | 4.5 (3.5, 5.8)            |  | 4.4 (3.5, 5.8)            |  | 4.4 (3.5, 5.8)            |
| <b>Wrinkle length</b>                       |  |                           |  |                           |  |                           |
| Mean (SD)                                   |  | 14870.5 (7746.4)          |  | 12963.6 (7517.7)          |  | 13946.9 (7690.7)          |
| Median (Q1, Q3)                             |  | 12829.0 (9318.0, 18579.5) |  | 10465.5 (7788.5, 15908.8) |  | 11543.0 (8385.0, 17661.0) |
| <b>Photoaging Glogau 4</b>                  |  |                           |  |                           |  |                           |
| 1                                           |  | 101 (26.6%)               |  | 85 (23.9%)                |  | 186 (25.3%)               |
| 2                                           |  | 182 (48.0%)               |  | 164 (46.1%)               |  | 346 (47.1%)               |
| 3                                           |  | 86 (22.7%)                |  | 91 (25.6%)                |  | 177 (24.1%)               |
| 4                                           |  | 10 (2.6%)                 |  | 16 (4.5%)                 |  | 26 (3.5%)                 |
| <b>Photoaging Glogau 2</b>                  |  |                           |  |                           |  |                           |
| 1                                           |  | 283 (74.7%)               |  | 249 (69.9%)               |  | 532 (72.4%)               |
| 2                                           |  | 96 (25.3%)                |  | 107 (30.1%)               |  | 203 (27.6%)               |
| <b>Photonumeric full-face wrinkle score</b> |  |                           |  |                           |  |                           |
| Small                                       |  | 367 (96.8%)               |  | 346 (97.2%)               |  | 713 (97.0%)               |
| Deep                                        |  | 12 (3.2%)                 |  | 10 (2.8%)                 |  | 22 (3.0%)                 |
| <b>Forehead wrinkles</b>                    |  |                           |  |                           |  |                           |
| Small                                       |  | 291 (76.8%)               |  | 198 (55.6%)               |  | 489 (66.5%)               |
| Deep                                        |  | 88 (23.2%)                |  | 158 (44.4%)               |  | 246 (33.5%)               |
| <b>Crow's feet</b>                          |  |                           |  |                           |  |                           |

|                                 |  |                   |  |                   |  |                   |
|---------------------------------|--|-------------------|--|-------------------|--|-------------------|
| Small                           |  | 324 (85.5%)       |  | 291 (81.7%)       |  | 615 (83.7%)       |
| Deep                            |  | 55 (14.5%)        |  | 65 (18.3%)        |  | 120 (16.3%)       |
| <b>Lip wrinkles</b>             |  |                   |  |                   |  |                   |
| Small                           |  | 358 (94.5%)       |  | 354 (99.4%)       |  | 712 (96.9%)       |
| Deep                            |  | 21 (5.5%)         |  | 2 (0.6%)          |  | 23 (3.1%)         |
| <b>Nasolabial folds</b>         |  |                   |  |                   |  |                   |
| Small                           |  | 297 (78.4%)       |  | 273 (76.7%)       |  | 570 (77.6%)       |
| Deep                            |  | 82 (21.6%)        |  | 83 (23.3%)        |  | 165 (22.4%)       |
| <b>Eyelid drooping</b>          |  |                   |  |                   |  |                   |
| Small                           |  | 272 (71.8%)       |  | 232 (65.2%)       |  | 504 (68.6%)       |
| Deep                            |  | 107 (28.2%)       |  | 124 (34.8%)       |  | 231 (31.4%)       |
| <b>Skin color (Fitzpatrick)</b> |  |                   |  |                   |  |                   |
| Light                           |  | 334 (88.1%)       |  | 326 (91.6%)       |  | 660 (89.8%)       |
| Dark                            |  | 45 (11.9%)        |  | 30 (8.4%)         |  | 75 (10.2%)        |
| <b>Pigmentation Spots</b>       |  |                   |  |                   |  |                   |
| 0 None                          |  | 17 (4.5%)         |  | 9 (2.5%)          |  | 26 (3.5%)         |
| 1 A few                         |  | 336 (88.7%)       |  | 331 (93.0%)       |  | 667 (90.7%)       |
| 2 Many                          |  | 26 (6.9%)         |  | 16 (4.5%)         |  | 42 (5.7%)         |
| <b>Telangiectasias</b>          |  |                   |  |                   |  |                   |
| 0 None                          |  | 205 (54.1%)       |  | 169 (47.5%)       |  | 374 (50.9%)       |
| 1 A few                         |  | 140 (36.9%)       |  | 136 (38.2%)       |  | 276 (37.6%)       |
| 2 Many                          |  | 34 (9.0%)         |  | 51 (14.3%)        |  | 85 (11.6%)        |
| <b>Lip height</b>               |  |                   |  |                   |  |                   |
| Mean (SD)                       |  | 1.4 (0.4)         |  | 1.3 (0.4)         |  | 1.4 (0.4)         |
| Median (Q1, Q3)                 |  | 1.4 (1.2, 1.7)    |  | 1.3 (1.0, 1.5)    |  | 1.4 (1.1, 1.6)    |
| Missing                         |  | 3 (0.8%)          |  | 2 (0.6%)          |  | 5 (0.7%)          |
| <b>Facial height</b>            |  |                   |  |                   |  |                   |
| Mean (SD)                       |  | 11.9 (0.9)        |  | 12.4 (1.4)        |  | 12.2 (1.2)        |
| Median (Q1, Q3)                 |  | 12.0 (11.5, 12.5) |  | 12.7 (11.5, 13.3) |  | 12.3 (11.5, 12.9) |
| Missing                         |  | 3 (0.8%)          |  | 2 (0.6%)          |  | 5 (0.7%)          |

**Supplementary Table 4.** The association between multiple facial skin aging traits and lifestyle factors, adjusted for age and sex.

| Variable                     | Wrinkle area |                  | Perceived Facial Age |                  | Glogau photoaging |                   |                 | Nasolabial folds |                   |                 | Drooping eyelids |                    |                 |
|------------------------------|--------------|------------------|----------------------|------------------|-------------------|-------------------|-----------------|------------------|-------------------|-----------------|------------------|--------------------|-----------------|
|                              | Std.B        | p                | Std.B                | p                | OR                | 95% CI            | p               | OR               | 95% CI            | p               | OR               | 95% CI             | p               |
| Age                          | <b>0.89</b>  | <b>7.48e-245</b> | <b>0.93</b>          | <b>2.82E-271</b> | <b>1.25</b>       | <b>1.21, 1.30</b> | <b>1.31e-37</b> | <b>1.10</b>      | <b>1.08, 1.11</b> | <b>7.14e-31</b> | 1.10             | 1.08, 1.11         | 1.08e-35        |
| Sex (Male/Female)            | <b>0.10</b>  | <b>7.60e-09</b>  | <b>0.12</b>          | <b>1.03E-14</b>  | <b>3.29</b>       | <b>1.87, 5.96</b> | <b>5.17e-05</b> | 1.33             | 0.89, 2.00        | 0.16            | <b>1.87</b>      | <b>1.27, 2.75</b>  | <b>0.002</b>    |
| Education                    |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| University degree/no         | 0.01         | 0.37             | <b>-0.06</b>         | <b>2.32E-04</b>  | <b>0.38</b>       | <b>0.21, 0.67</b> | <b>0.0009</b>   | 0.73             | 0.49, 1.11        | 0.14            | <b>0.54</b>      | <b>0.37, 0.80</b>  | <b>0.002</b>    |
| Socioeconomic status (SES)   |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| High/Medium vs. Low          | 0.004        | 0.78             | 0.003                | 0.86             | <b>0.29</b>       | <b>0.09, 0.94</b> | <b>0.04</b>     | 0.75             | 0.30, 1.94        | 0.54            | <b>0.38</b>      | <b>0.15, 0.94</b>  | <b>0.04</b>     |
| Residence                    |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| City<100K citizens / Village | -0.01        | 0.51             | 0.006                | 0.78             | 1                 | 0.42, 2.41        | 0.10            | 1.32             | 0.66, 2.66        | 0.44            | 1.09             | 0.59, 2.01         | 0.77            |
| City>100K citizens / Village | -0.0004      | 0.98             | -0.02                | 0.25             | <b>0.43</b>       | <b>0.20, 0.90</b> | <b>0.03</b>     | 1.03             | 0.59, 1.84        | 0.92            | <b>0.45</b>      | <b>0.27, 0.74</b>  | <b>0.002</b>    |
| Type of job                  |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| SM/Manual                    | 0.002        | 0.94             | -0.04                | 0.17             | <b>0.58</b>       | <b>0.15, 0.78</b> | <b>0.01</b>     | 1.28             | 0.68, 2.48        | 0.45            | <b>0.50</b>      | <b>0.27, 0.91</b>  | <b>0.02</b>     |
| LSM/Manual                   | 0.01         | 0.65             | <b>-0.08</b>         | <b>0.002</b>     | 0.72              | 0.20, 0.99        | 0.05            | 0.88             | 0.46, 1.69        | 0.69            | 0.57             | 0.32, 1.00         | 0.05            |
| Lifestyle factors            |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Stress (Yes/No)              | -0.031       | 0.09             | <b>0.05</b>          | <b>0.002</b>     | <b>3.20</b>       | <b>1.35, 7.57</b> | <b>0.008</b>    | 1.21             | 0.59, 2.48        | 0.60            | <b>1.89</b>      | <b>1.07, 3.33</b>  | <b>0.03</b>     |
| Yoga (Yes/No)                | 0.0007       | 0.97             | -0.02                | 0.11             | 0.49              | 0.17, 1.33        | 0.18            | 1.07             | 0.51, 2.15        | 0.86            | 0.76             | 0.37, 1.49         | 0.43            |
| PA (Active/Inactive)         | 0.02         | 0.29             | -0.001               | 0.93             | <b>0.50</b>       | <b>0.28, 0.91</b> | <b>0.02</b>     | 0.74             | 0.47, 1.18        | 0.21            | 0.86             | 0.56, 1.35         | 0.52            |
| Strengthening/Aerobic        | 0.03         | 0.26             | <b>0.06</b>          | <b>0.002</b>     | 1.14              | 4.46, 2.84        | 0.78            | 0.62             | 0.27, 1.33        | 0.24            | 0.83             | 0.43, 1.57         | 0.58            |
| Yoga or balance/Aerobic      | -0.002       | 0.92             | -0.02                | 0.29             | 2.18              | 7.27, 6.60        | 0.16            | 2.42             | 1.03, 5.62        | 0.04            | 1.55             | 0.66, 3.61         | 0.31            |
| Walk or Running (Yes/No)     | 0.002        | 0.94             | -0.03                | 0.07             | <b>0.37</b>       | <b>1.57, 8.21</b> | <b>0.02</b>     | 0.75             | 0.40, 1.37        | 0.36            | <b>0.53</b>      | <b>0.29, 0.94</b>  | <b>0.03</b>     |
| Sleeping hours               | -0.009       | 0.59             | -0.02                | 0.27             | 0.97              | 0.77, 1.24        | 0.83            | 0.91             | 0.76, 1.08        | 0.26            | 1.08             | 0.92, 1.27         | 0.36            |
| BMI                          | -0.003       | 0.87             | 0.01                 | 0.54             | 1.05              | 1.00, 1.11        | 0.06            | 1.0              | 0.95, 1.04        | 0.82            | <b>1.12</b>      | <b>1.07, 1.17</b>  | <b>4.01e-07</b> |
| Smoking                      |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Former smoker/Never          | 0.008        | 0.66             | 0.01                 | 0.45             | 0.98              | 0.50, 1.89        | 0.94            | 1.32             | 0.81, 2.15        | 0.26            | 1.44             | 0.90, 2.28         | 0.12            |
| Current smoker/Never         | 0.02         | 0.30             | 0.02                 | 0.16             | 1.55              | 0.80, 3.01        | 0.19            | 1.40             | 0.83, 2.36        | 0.21            | 1.22             | 0.76, 1.95         | 0.41            |
| Alcohol drink                |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Occasionally/Never           | 0.002        | 0.92             | 0.006                | 0.78             | 1.44              | 0.59, 3.59        | 0.42            | 0.82             | 0.45, 1.50        | 0.51            | 1.21             | 0.67, 2.24         | 0.53            |
| Frequently/Never             | -0.01        | 0.62             | -0.02                | 0.23             | 1.15              | 0.37, 3.53        | 0.81            | 0.88             | 0.39, 1.96        | 0.75            | 0.96             | 0.43, 2.10         | 0.91            |
| Type of Diet                 |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Vegetarian/Varied            | 0.009        | 0.60             | <b>-0.04</b>         | <b>0.01</b>      | 0.73              | 0.11, 3.14        | 0.70            | 0.71             | 0.15, 2.30        | 0.61            | 1.10             | 0.36, 2.94         | 0.86            |
| Protein/Varied               | 0.02         | 0.19             | 0.03                 | 0.05             | 1.65              | 0.21, 8.62        | 0.58            | NA               | NA                | NA              | 0.50             | 0.08, 1.91         | 0.37            |
| Sugar intake                 |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Medium/low                   | <b>-0.08</b> | <b>0.004</b>     | -0.02                | 0.34             | 1.07              | 0.39, 3.13        | 0.90            | 1.09             | 0.51, 2.47        | 0.84            | <b>3.19</b>      | <b>1.43, 7.83</b>  | <b>0.007</b>    |
| High/low                     | <b>-0.06</b> | <b>0.03</b>      | <b>-0.05</b>         | <b>0.02</b>      | 1.15              | 0.36, 3.88        | 0.81            | 1.08             | 0.45, 2.69        | 0.87            | 2.56             | 1.04, 6.81         | 0.05            |
| Water per day                | -0.002       | 0.92             | -0.0009              | 0.95             | 1.27              | 0.58, 2.85        | 0.56            | 1.11             | 0.61, 2.08        | 0.73            | 1.60             | 0.89, 2.97         | 1.25            |
| Cups of coffee per day       |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Small/Non                    | <b>-0.05</b> | <b>0.02</b>      | 0.01                 | 0.58             | 1.31              | 0.63, 2.76        | 0.48            | 0.92             | 0.54, 1.58        | 0.77            | 1.23             | 0.75, 2.03         | 0.42            |
| Large/Non                    | 0.0005       | 0.98             | 0.02                 | 0.39             | 1.75              | 0.76, 4.09        | 0.19            | 0.86             | 0.45, 1.63        | 0.65            | 0.65             | 0.36, 1.17         | 0.15            |
| Skin condition               |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Skin color (Dark/Light)      | <b>0.04</b>  | <b>0.01</b>      | <b>0.04</b>          | <b>0.02</b>      | 0.58              | 0.22, 1.48        | 0.27            | 1.18             | 0.60, 2.24        | 0.63            | 0.92             | 0.48, 1.71         | 0.79            |
| Tanning (Freq./ Rarely)      | 0.02         | 0.36             | <b>0.04</b>          | <b>0.009</b>     | 0.99              | 0.57, 1.70        | 0.96            | <b>1.80</b>      | <b>1.19, 2.75</b> | <b>0.006</b>    | 1.24             | 0.85, 1.83         | 0.26            |
| Solarium                     |              |                  |                      |                  |                   |                   |                 |                  |                   |                 |                  |                    |                 |
| Former solarium/Never        | -0.03        | 0.15             | 0.02                 | 0.19             | 1.34              | 0.67, 2.66        | 0.40            | 1.22             | 0.71, 2.08        | 0.46            | 1.16             | 0.73, 1.84         | 0.53            |
| Current solarium/Never       | -0.005       | 0.79             | <b>0.05</b>          | <b>0.002</b>     | 2.31              | 0.57, 8.40        | 0.22            | <b>2.58</b>      | <b>0.99, 6.19</b> | <b>0.04</b>     | <b>0.10</b>      | <b>0.006, 0.52</b> | <b>0.03</b>     |

| Variable                   | Photonumeric full-face wrinkle score |                   |                 | Forehead wrinkles |                   |                 | Crow's feet |                   |                 | Lip wrinkles |                   |                 |
|----------------------------|--------------------------------------|-------------------|-----------------|-------------------|-------------------|-----------------|-------------|-------------------|-----------------|--------------|-------------------|-----------------|
|                            | OR                                   | 95% CI            | p               | OR                | 95% CI            | p               | OR          | 95% CI            | p               | OR           | 95% CI            | p               |
| Age                        | <b>1.14</b>                          | <b>1.10, 1.20</b> | <b>7.91e-09</b> | <b>1.07</b>       | <b>1.05, 1.08</b> | <b>2.89e-23</b> | <b>1.09</b> | <b>1.07, 1.11</b> | <b>1.18e-24</b> | <b>1.21</b>  | <b>1.14, 1.29</b> | <b>4.08e-09</b> |
| Sex (Male/Female)          | 0.77                                 | 0.30, 1.95        | 0.59            | 3.77              | 2.64, 5.44        | 6.36e-13        | 1.57        | 1.01, 2.46        | 0.044           | 0.04         | 0.01, 0.18        | 1.50e-04        |
| Education                  |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| University degree/no       | 1.09                                 | 0.43, 2.86        | 0.85            | 0.90              | 0.63, 1.29        | 0.55            | 0.80        | 0.51, 1.25        | 0.32            | 1.24         | 0.45, 3.51        | 0.67            |
| Socioeconomic status (SES) |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| High/Medium vs. Low        | 0.68                                 | 0.15, 4.3         | 0.65            | 1.07              | 0.45, 2.64        | 0.89            | 0.82        | 0.32, 2.33        | 0.69            | 1.46         | 0.27, 11.88       | 0.68            |
| Residence                  |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| City<100K/ Village         | 6.67                                 | 0.96, 134         | 0.10            | 0.79              | 0.43, 1.44        | 0.44            | 0.95        | 0.47, 1.94        | 0.90            | 0.22         | 0.01, 2.04        | 0.24            |
| City>100K/ Village         | 2.85                                 | 0.53, 52.9        | 0.32            | 0.92              | 0.57, 1.48        | 0.72            | <b>0.44</b> | <b>0.24, 0.79</b> | <b>0.006</b>    | 0.67         | 0.19, 2.71        | 0.54            |
| Type of job                |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| SM/Manual                  | 0.72                                 | 0.08, 6.86        | 0.76            | 0.81              | 0.48, 1.39        | 0.44            | 0.76        | 0.36, 1.64        | 0.48            | 0.96         | 0.08, 22.7        | 0.98            |
| LSM/Manual                 | 1.03                                 | 0.17, 8.40        | 0.97            | 0.90              | 0.55, 1.49        | 0.69            | 1.07        | 0.53, 2.24        | 0.84            | 1.79         | 0.22, 39.0        | 0.63            |
| Lifestyle factor           |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Stress (Yes/No)            | NA                                   | NA                | NA              | 0.79              | 0.45, 1.37        | 0.40            | <b>3.04</b> | <b>1.47, 6.29</b> | <b>0.003</b>    | NA           | NA                | NA              |
| Yoga (Yes/No)              | 1.06e-07                             | 1.81e-147, 2.17   | 0.99            | 0.77              | 0.39, 1.46        | 0.44            | <b>0.30</b> | <b>0.08, 0.81</b> | <b>0.03</b>     | 0.16         | 0.01, 1.11        | 0.12            |
| PA (Yes/No)                | 1.15                                 | 0.44, 3.44        | 0.78            | 0.77              | 0.50, 1.17        | 0.22            | 0.73        | 0.45, 1.20        | 0.20            | 0.57         | 0.20, 1.65        | 0.29            |
| Strengthening/Aerobic      | 0.91                                 | 0.04, 6.63        | 0.94            | 1.45              | 0.87, 2.42        | 0.16            | 0.55        | 0.20, 1.30        | 0.19            | 1.95         | 0.22, 14.01       | 0.51            |
| Yoga or balance/Aerobic    | 1.66                                 | 2.21, 8.59        | 0.57            | 1.06              | 0.43, 2.48        | 0.89            | 0.88        | 0.32, 2.27        | 0.80            | 2.12         | 0.35, 11.51       | 0.39            |
| Walk or Running (Yes/No)   | 0.50                                 | 0.10, 1.96        | 0.35            | <b>0.59</b>       | <b>0.36, 0.96</b> | <b>0.04</b>     | <b>0.29</b> | <b>0.13, 0.62</b> | <b>0.002</b>    | 0.28         | 0.03, 1.52        | 0.18            |
| Sleeping hours             | 1.12                                 | 0.79, 1.59        | 0.51            | 0.90              | 0.77, 1.05        | 0.18            | 1.02        | 0.85, 1.22        | 0.85            | 0.73         | 0.48, 1.07        | 0.12            |
| BMI                        | 0.92                                 | 0.80, 1.04        | 0.20            | 1.04              | 1.00, 1.08        | 0.07            | 1.04        | 0.99, 1.09        | 0.10            | 0.85         | 0.72, 0.99        | 0.05            |
| Smoking                    |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Former smoker/Never        | <b>4.13</b>                          | <b>1.41, 13.3</b> | <b>0.01</b>     | 0.91              | 0.58, 1.40        | 0.66            | 0.97        | 0.57, 1.64        | 0.92            | 2.23         | 0.67, 7.57        | 0.19            |
| Current smoker/Never       | <b>6.30</b>                          | <b>1.55, 26.1</b> | <b>0.009</b>    | 0.81              | 0.52, 1.25        | 0.34            | 1.07        | 0.58, 1.92        | 0.81            | <b>4.75</b>  | <b>1.14, 20.0</b> | <b>0.03</b>     |
| Alcohol drink              |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Occasionally/Never         | 1.10                                 | 0.37, 3.75        | 0.87            | 0.67              | 0.39, 1.14        | 0.14            | 1.48        | 0.76, 2.98        | 0.26            | 3.44         | 0.89, 17.8        | 0.10            |
| Frequently/Never           | 0.70                                 | 0.03, 5.28        | 0.76            | 0.82              | 0.40, 1.66        | 0.58            | 1.12        | 0.43, 2.84        | 0.81            | 6.97         | 0.64, 68.6        | 0.09            |
| Type of Diet               |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Vegetarian/ Varied         | 2.46e-7                              | 2.38e-260, 4.35   | 0.99            | 1.03              | 0.35, 2.73        | 0.95            | 0.72        | 0.11, 2.71        | 0.67            | NA           | NA                | NA              |
| Protein/ Varied            | 1.24e-06                             | 1.72e-295, 1.80   | 0.99            | 1.17              | 0.39, 3.14        | 0.77            | NA          | NA                | NA              | NA           | NA                | NA              |
| Sugar intake               |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Medium/ Low                | 1.20                                 | 0.21, 22.8        | 0.86            | 0.73              | 0.40, 1.37        | 0.32            | 2.27        | 0.89, 7.07        | 0.12            | 0.53         | 0.10, 4.05        | 0.48            |
| High/ Low                  | 1.20                                 | 0.17, 24.3        | 0.88            | 0.69              | 0.33, 1.43        | 0.31            | 1.29        | 0.44, 4.42        | 0.66            | 0.09         | 0.01, 0.99        | 0.04            |
| Water per day              | 0.52                                 | 0.19, 1.63        | 0.23            | 0.92              | 0.54, 1.60        | 0.77            | 1.01        | 0.54, 1.97        | 0.98            | 0.69         | 0.21, 2.55        | 0.55            |
| Cups of coffee per day     |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Small/Non                  | 1.22                                 | 0.40, 4.58        | 0.75            | 1.46              | 0.91, 2.37        | 0.12            | 0.72        | 0.41, 1.29        | 0.26            | 1.87         | 0.43, 13.4        | 0.46            |
| Large/Non                  | 0.30                                 | 0.01, 2.31        | 0.31            | 1.13              | 0.66, 1.95        | 0.65            | 1.02        | 0.52, 2.02        | 0.95            | 3.14         | 0.48, 27.8        | 0.25            |
| Skin condition             |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Skin color (Dark/Light)    | 1.10                                 | 0.23, 3.81        | 0.90            | 1.15              | 0.64, 2.03        | 0.63            | 0.64        | 0.28, 1.37        | 0.28            | 0.61         | 0.08, 2.70        | 0.56            |
| Tanning (Freq/ Rarely)     | 0.70                                 | 0.23, 1.90        | 0.50            | 1.06              | 0.75, 1.51        | 0.74            | 1.04        | 0.66, 1.64        | 0.87            | 0.86         | 0.24, 2.70        | 0.80            |
| Solarium                   |                                      |                   |                 |                   |                   |                 |             |                   |                 |              |                   |                 |
| Former solarium/ Never     | 1.13                                 | 0.16, 4.91        | 0.88            | 1.25              | 0.80, 1.94        | 0.32            | 1.10        | 0.58, 1.99        | 0.77            | 0.43         | 0.02, 2.64        | 0.44            |
| Current solarium/ Never    | NA                                   | NA                | NA              | 1.94              | 0.87, 4.12        | 0.09            | 1.07        | 0.24, 3.33        | 0.92            | NA           | NA                | NA              |

| Variable                   | Subjective aging rate |                   |                 | Pigmentation spots |                    |               | Telangiectasias |                   |                 | Facial height |                 | Lip height   |                 |
|----------------------------|-----------------------|-------------------|-----------------|--------------------|--------------------|---------------|-----------------|-------------------|-----------------|---------------|-----------------|--------------|-----------------|
|                            | OR                    | 95% CI            | p               | OR                 | 95% CI             | p             | OR              | 95% CI            | p               | Std.B         | p               | Std.B        | p               |
| Age                        | 0.99                  | 0.98, 1.01        | 0.33            | <b>1.08</b>        | <b>1.04, 1.12</b>  | <b>1.0e-4</b> | <b>1.06</b>     | <b>1.04, 1.07</b> | <b>1.53e-19</b> | <b>0.24</b>   | <b>6.94e-11</b> | -0.33        | 1.36e-20        |
| Sex (Male/Female)          | 1.34                  | 1.00, 1.81        | 0.05            | <b>2.44</b>        | <b>1.07, 5.96</b>  | <b>0.04</b>   | <b>1.59</b>     | <b>1.16, 2.19</b> | <b>3.83e-03</b> | <b>0.22</b>   | <b>2.04e-09</b> | -0.22        | <b>4.33e-10</b> |
| Education                  |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| University degree/no       | <b>0.64</b>           | <b>0.46, 0.89</b> | <b>0.007</b>    | 0.53               | 0.17, 1.36         | 0.22          | 0.84            | 0.61, 1.17        | 0.31            | <b>0.12</b>   | <b>9.0e-04</b>  | <b>0.08</b>  | <b>0.02</b>     |
| Socioeconomic status (SES) |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| High/Medium vs. Low        | <b>0.27</b>           | <b>0.13, 0.56</b> | <b>4.19e-04</b> | 0.60               | 0.095, 2.09        | 0.49          | 0.64            | 0.31, 1.31        | 0.22            | 0.04          | 0.25            | 0.04         | 0.24            |
| Residence                  |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| City<100K/ Village         | <b>0.50</b>           | <b>0.28, 0.87</b> | <b>1.46e-02</b> | 0.93               | 0.17, 5.21         | 0.93          | 0.88            | 0.52, 1.50        | 0.64            | -0.005        | 0.92            | -0.01        | 0.76            |
| City>100K/ Village         | <b>0.36</b>           | <b>0.23, 0.57</b> | <b>1.77e-05</b> | 0.55               | 0.13, 1.68         | 0.35          | 0.89            | 0.59, 1.36        | 0.60            | 0.06          | 0.18            | 0.04         | 0.38            |
| Type of job                |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| SM/Manual                  | <b>0.48</b>           | <b>0.30, 0.78</b> | <b>0.003</b>    | 0.35               | 0.09, 1.11         | 0.10          | <b>0.58</b>     | <b>0.35, 0.95</b> | <b>0.03</b>     | 0.05          | 0.67            | 0.07         | 0.18            |
| LSM/Manual                 | 0.64                  | 0.40, 1.02        | 0.06            | 1.30               | 0.31, 4.77         | 0.70          | 0.80            | 0.51, 1.26        | 0.34            | <b>0.19</b>   | <b>0.0002</b>   | 0.08         | 0.10            |
| Lifestyle factor           |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Stress (Yes/No)            | 1.55                  | 0.96, 2.53        | 0.08            | NA                 | NA                 | NA            | 1.11            | 0.70, 1.77        | 0.66            | <b>-0.46</b>  | <b>1.72e-37</b> | <b>-0.23</b> | <b>3.78e-10</b> |
| Yoga (Yes/No)              | <b>0.33</b>           | <b>0.19, 0.55</b> | <b>4.30e-05</b> | 0.98               | 0.31, 4.33         | 0.97          | 1.01            | 0.58, 1.73        | 0.98            | 0.04          | 0.31            | 0.05         | 0.20            |
| Physical activity (Yes/No) | <b>0.61</b>           | <b>0.41, 0.89</b> | <b>0.01</b>     | 2.09               | 0.77, 5.17         | 0.13          | <b>0.60</b>     | <b>0.40, 0.89</b> | <b>0.01</b>     | -0.004        | 0.91            | -0.05        | 0.18            |
| Strengthening/Aerobic      | 0.71                  | 0.46, 1.09        | 0.11            | <b>6.65</b>        | <b>1.75, 43.68</b> | <b>0.02</b>   | 0.77            | 0.49, 1.21        | 0.26            | 0.28          | 7.84e-09        | 0.02         | 0.34            |
| Yoga or balance/Aerobic    | 0.74                  | 0.37, 1.46        | 0.38            | 1.71               | 0.28, 32.95        | 0.63          | 1.18            | 0.57, 2.43        | 0.66            | 0.08          | 0.07            | 0.01         | 0.82            |
| Walk or Running (Yes/No)   | 1.31                  | 0.88, 1.98        | 0.19            | 1.07               | 0.35, 3.96         | 0.91          | 0.67            | 0.43, 1.02        | 0.07            | <b>-0.17</b>  | <b>0.0002</b>   | -0.03        | 0.56            |
| Sleeping hours             | 0.88                  | 0.77, 1.00        | 0.05            | <b>1.56</b>        | <b>1.09, 2.24</b>  | <b>0.01</b>   | 0.88            | 0.77, 1.01        | 0.07            | -0.01         | 0.71            | 0.06         | 0.09            |
| BMI                        | <b>0.11</b>           | <b>1.07, 1.15</b> | <b>2.80e-07</b> | 0.98               | 0.89, 1.08         | 0.65          | <b>1.09</b>     | <b>1.05, 1.14</b> | <b>7.74e-06</b> | 0.05          | 0.21            | -0.01        | 0.74            |
| Smoking                    |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Former smoker/Never        | 0.95                  | 0.65, 1.39        | 0.79            | <b>0.27</b>        | <b>0.09, 0.80</b>  | <b>0.02</b>   | 1.26            | 0.84, 1.90        | 0.26            | -0.07         | 0.08            | -0.03        | 0.39            |
| Current smoker/Never       | 1.44                  | 0.99, 2.12        | 0.06            | <b>0.31</b>        | <b>0.11, 0.80</b>  | <b>0.02</b>   | 1.11            | 0.75, 1.63        | 0.60            | -0.03         | 0.37            | 0.03         | 0.42            |
| Alcohol drink              |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Occasionally/ Never        | 1.12                  | 0.70, 1.79        | 0.63            | 0.80               | 0.12, 2.92         | 0.77          | 0.70            | 0.42, 1.16        | 0.17            | -0.03         | 0.55            | 0.007        | 0.88            |
| Frequently/ Never          | 0.89                  | 0.48, 1.66        | 0.72            | 0.44               | 0.06, 2.38         | 0.36          | <b>0.47</b>     | <b>0.24, 0.92</b> | <b>0.03</b>     | 0.02          | 0.69            | 0.05         | 0.29            |
| Type of Diet               |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Vegetarian/ Varied         | <b>0.29</b>           | <b>0.11, 0.70</b> | <b>0.008</b>    | 0.87               | 0.16, 16.14        | 0.89          | 2.05            | 0.86, 5.14        | 0.11            | 0.05          | 0.18            | 0.05         | 0.12            |
| Protein/ Varied            | 0.55                  | 0.22, 1.37        | 0.19            | NA                 | NA                 | NA            | 1.29            | 0.50, 3.25        | 0.60            | 0.03          | 0.48            | 0.05         | 0.16            |
| Sugar intake               |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Medium/ Low                | 0.94                  | 0.53, 1.63        | 0.82            | 2.50e-07           | 2.74e-108, 3e+11   | 0.99          | 0.77            | 0.43, 1.36        | 0.37            | -0.05         | 0.39            | -0.02        | 0.78            |
| High/ Low                  | 0.95                  | 0.49, 1.81        | 0.89            | NA                 | NA                 | NA            | 0.75            | 0.38, 1.45        | 0.39            | -0.04         | 0.52            | 0.06         | 0.30            |
| Water per day (>2/<2)      | 0.84                  | 0.52, 1.34        | 0.46            | 1.65               | 0.46, 4.69         | 0.39          | 1.60            | 0.97, 2.66        | 0.07            | 0.001         | 0.97            | 0.02         | 0.50            |
| Cups of coffee per day     |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Small/Non                  | 0.92                  | 0.62, 1.37        | 0.69            | 0.82               | 0.22, 2.38         | 0.73          | 1.17            | 0.77, 1.78        | 0.48            | 0.07          | 0.14            | -0.06        | 0.20            |
| Large/Non                  | 1.28                  | 0.80, 2.03        | 0.31            | 0.72               | 0.18, 2.51         | 0.62          | 1.17            | 0.72, 1.88        | 0.53            | 0.04          | 0.39            | 0.009        | 0.84            |
| Skin condition             |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Skin color (Dark/Light)    | 0.71                  | 0.44, 1.16        | 0.17            | 1.46               | 0.41, 9.34         | 0.62          | <b>0.46</b>     | <b>0.26, 0.79</b> | <b>5.16e-03</b> | 0.03          | 0.35            | 0.02         | 0.56            |
| Tanning (Freq./ Rarely)    | 0.80                  | 0.59, 1.08        | 0.15            | 2.01               | 0.88, 5.03         | 0.11          | 1.05            | 0.77, 1.44        | 0.77            | -0.02         | 0.63            | -0.002       | 0.96            |
| Solarium                   |                       |                   |                 |                    |                    |               |                 |                   |                 |               |                 |              |                 |
| Former solarium/ Never     | 0.76                  | 0.53, 1.11        | 0.15            | 0.87               | 0.38, 2.10         | 0.75          | 1.40            | 0.96, 2.04        | 0.08            | 0.03          | 0.37            | 0.06         | 0.09            |
| Current solarium/ Never    | <b>0.39</b>           | <b>0.20, 0.75</b> | <b>0.005</b>    | NA                 | NA                 | NA            | 0.62            | 0.28, 1.28        | 0.21            | <b>0.09</b>   | <b>0.01</b>     | 0.05         | 0.18            |

Glogau photoging: a two-stage categorization was used, comparing categories III and IV vs. categories I and II (reference); Nasolabial folds, eyelid drooping, photonumeric full-face wrinkles, forehead wrinkles, crow's feet, lip wrinkles: deep wrinkles vs. small wrinkles (reference) were analysed; subjective aging rate was measured on a 3-point scale: 0 (younger than real age), 1 (as real age) and 2 (older than real age); wrinkle area, facial perceived age, facial height and lip height were analysed on a continuous scale.

Type of job: Sedentary mental (SM), Long hours Sedentary Mental (LSM), Manual (M); Cups of coffee per day: small (1-2 cups/day), large ( $\geq 3$  cups/day); Stress vulnerability: measured on a 3-point scale: low, medium, high

Std.B: the standardized beta regression coefficient of the respective variable from the linear regression model applied for continuous traits; OR: Odds ratio from the logistic regression applied for categorical traits, 95% CI: confidence interval. p: significant p-values ( $<0.05$ ) are marked with bold. Due to the small number of observations in some categories, the results were not estimated (NA) because of instability in the model's results. **Results of association were adjusted for age and sex.**

**Supplementary Table 9.** Associations between selected facial skin aging traits, including photonumeric wrinkle classifications, Glogau photoaging, nasolabial folds, and eyelid drooping, facial height and lip height with various measures of epigenetic aging.

|                                                                             | Photonumeric full-face wrinkle score<br>N=735 |                |      | Forehead wrinkles<br>N=735 |             |      | Crow's feet<br>N=735 |                   |             | Lip wrinkles<br>N=735 |                   |             |
|-----------------------------------------------------------------------------|-----------------------------------------------|----------------|------|----------------------------|-------------|------|----------------------|-------------------|-------------|-----------------------|-------------------|-------------|
|                                                                             | OR                                            | 95% CI         | p    | OR                         | 95% CI      | p    | OR                   | 95% CI            | p           | OR                    | 95% CI            | p           |
| <b>Model 1 (age and sex adjusted)</b>                                       |                                               |                |      |                            |             |      |                      |                   |             |                       |                   |             |
| DNAm age Horvath                                                            | 1.02                                          | 0.92, 1.12     | 0.70 | 0.98                       | 0.94, 1.02  | 0.44 | 0.98                 | 0.93, 1.03        | 0.43        | 0.98                  | 0.87, 1.11        | 0.80        |
| DNAm age Hannum                                                             | 0.97                                          | 0.87, 1.08     | 0.55 | 1.02                       | 0.97, 1.07  | 0.49 | 1.02                 | 0.96, 1.08        | 0.58        | 0.96                  | 0.85, 1.09        | 0.53        |
| DNAm age Skin&Blood                                                         | 1.05                                          | 0.92, 1.19     | 0.45 | 1.02                       | 0.96, 1.07  | 0.58 | 1.07                 | 1.00, 1.15        | 0.05        | 0.88                  | 0.75, 1.01        | 0.07        |
| IEAA                                                                        | 1.03                                          | 0.93, 1.14     | 0.53 | 0.99                       | 0.95, 1.03  | 0.57 | 0.98                 | 0.93, 1.03        | 0.42        | 0.97                  | 0.86, 1.10        | 0.64        |
| EEAA                                                                        | 0.97                                          | 0.89, 1.06     | 0.55 | 1.01                       | 0.98, 1.05  | 0.49 | 1.01                 | 0.96, 1.05        | 0.77        | 0.98                  | 0.89, 1.08        | 0.66        |
| PhenoAgeAccel                                                               | 1.03                                          | 0.95, 1.12     | 0.42 | 0.98                       | 0.95, 1.01  | 0.26 | 1.01                 | 0.97, 1.05        | 0.57        | 1.04                  | 0.95, 1.14        | 0.37        |
| GrimAgeAccel                                                                | 1.06                                          | 0.94, 1.18     | 0.29 | 1.00                       | 0.95, 1.05  | 0.91 | 1.03                 | 0.97, 1.09        | 0.31        | <b>1.13</b>           | <b>1.01, 1.26</b> | <b>0.03</b> |
| FitAgeAccel                                                                 | 1.07                                          | 0.96, 1.19     | 0.23 | 1.03                       | 0.98, 1.08  | 0.26 | 0.99                 | 0.93, 1.04        | 0.61        | 1.07                  | 0.96, 1.20        | 0.22        |
| PACE                                                                        | 10.10                                         | 0.10, 891.04   | 0.31 | 2.36                       | 0.42, 13.27 | 0.33 | 4.02                 | 0.45, 35.76       | 0.21        | NA                    | NA                | NA          |
| PoAm                                                                        | 0.24                                          | 0.0002, 176.81 | 0.68 | 2.75                       | 0.24, 31.87 | 0.42 | 10.51                | 0.47, 229.90      | 0.14        | NA                    | NA                | NA          |
| Zhang MRS                                                                   | 0.67                                          | 0.16, 2.60     | 0.57 | 1.28                       | 0.75, 2.18  | 0.37 | 0.93                 | 0.47, 1.83        | 0.84        | 1.90                  | 0.47, 7.67        | 0.36        |
| DNAmTL                                                                      | 0.30                                          | 0.02, 3.81     | 0.36 | 0.88                       | 0.31, 2.52  | 0.81 | 0.59                 | 0.16, 2.12        | 0.42        | 0.04                  | 0.002, 0.79       | 0.04        |
| <b>Model 2 (adjusted for age, sex, lifestyle and blood cell proportion)</b> |                                               |                |      |                            |             |      |                      |                   |             |                       |                   |             |
| IEAA                                                                        | 1.02                                          | 0.91, 1.14     | 0.70 | 0.99                       | 0.95, 1.03  | 0.64 | 0.97                 | 0.92, 1.03        | 0.31        | 0.96                  | 0.83, 1.09        | 0.55        |
| EEAA                                                                        | 0.99                                          | 0.89, 1.10     | 0.83 | 1.02                       | 0.98, 1.07  | 0.32 | 1.02                 | 0.97, 1.08        | 0.50        | 0.94                  | 0.82, 1.07        | 0.38        |
| Skin&BloodAgeAccel                                                          | 1.03                                          | 0.89, 1.19     | 0.67 | 1.02                       | 0.97, 1.08  | 0.43 | <b>1.08</b>          | <b>1.00, 1.16</b> | <b>0.04</b> | <b>0.81</b>           | <b>0.67, 0.96</b> | <b>0.02</b> |
| PhenoAgeAccel                                                               | 1.04                                          | 0.96, 1.14     | 0.33 | 0.97                       | 0.94, 1.01  | 0.15 | 1.02                 | 0.98, 1.07        | 0.35        | 1.06                  | 0.96, 1.18        | 0.28        |
| GrimAgeAccel                                                                | 1.01                                          | 0.88, 1.15     | 0.91 | 1.00                       | 0.95, 1.07  | 0.89 | 1.07                 | 0.99, 1.15        | 0.07        | 1.09                  | 0.94, 1.27        | 0.26        |
| FitAgeAccel                                                                 | 1.02                                          | 0.90, 1.16     | 0.76 | 1.05                       | 0.99, 1.10  | 0.08 | 0.99                 | 0.93, 1.06        | 0.79        | 1.01                  | 0.88, 1.16        | 0.86        |
| PACE                                                                        | 8.23                                          | 0.04, 1589.37  | 0.44 | 2.29                       | 0.36, 14.80 | 0.38 | 6.64                 | 0.60, 74.12       | 0.12        | NA                    | NA                | NA          |
| PoAm                                                                        | 0.01                                          | 6.9e-07, 24.00 | 0.24 | 2.94                       | 0.17, 53.30 | 0.46 | 42.44                | 0.98, 1964.22     | 0.05        | NA                    | NA                | NA          |
| Zhang MRS                                                                   | 0.68                                          | 0.08, 5.63     | 0.73 | 1.34                       | 0.59, 3.05  | 0.49 | 1.47                 | 0.52, 4.19        | 0.47        | 3.39                  | 0.29, 40.98       | 0.33        |
| DNAmTL                                                                      | 0.53                                          | 0.03, 10.29    | 0.68 | 0.70                       | 0.22, 2.23  | 0.54 | 0.47                 | 0.11, 1.94        | 0.30        | 0.05                  | 0.001, 1.53       | 0.10        |

|                                                                             | Facial height<br>N=730 |      | Lip height<br>N=730 |      | Glogau photoaging<br>N=735 |                   |             | Nasolabial folds<br>N=735 |            |      | Eyelid drooping<br>N=735 |            |      |
|-----------------------------------------------------------------------------|------------------------|------|---------------------|------|----------------------------|-------------------|-------------|---------------------------|------------|------|--------------------------|------------|------|
|                                                                             | Std.B                  | P    | Std.B               | p    | OR                         | 95% CI            | p           | OR                        | 95% CI     | p    | OR                       | 95% CI     | p    |
| <b>Model 1 (age and sex adjusted)</b>                                       |                        |      |                     |      |                            |                   |             |                           |            |      |                          |            |      |
| DNAm age Horvath                                                            | -0.05                  | 0.62 | -0.03               | 0.77 | 0.97                       | 0.91,1.03         | 0.34        | 0.98                      | 0.94, 1.03 | 0.39 | 1.00                     | 0.96, 1.05 | 0.86 |
| DNAm age Hannum                                                             | -0.08                  | 0.51 | 0.01                | 0.96 | 1.01                       | 0.94,1.08         | 0.81        | 1.02                      | 0.96, 1.07 | 0.54 | 0.99                     | 0.94, 1.04 | 0.67 |
| DNAm age Skin&Blood                                                         | 0.13                   | 0.44 | 0.09                | 0.57 | 0.93                       | 0.85,1.02         | 0.15        | 1.00                      | 0.94, 1.07 | 0.92 | 1.00                     | 0.95, 1.07 | 0.89 |
| IEAA                                                                        | 0.01                   | 0.78 | 0.00                | 0.97 | 0.95                       | 0.89,1.02         | 0.16        | 0.97                      | 0.92, 1.01 | 0.17 | 1.00                     | 0.95, 1.04 | 0.85 |
| EEAA                                                                        | -0.02                  | 0.54 | -0.01               | 0.80 | 1.02                       | 0.96, 1.08        | 0.55        | 1.02                      | 0.97, 1.06 | 0.45 | 1.00                     | 0.96, 1.04 | 0.91 |
| PhenoAgeAccel                                                               | 0.02                   | 0.49 | 0.02                | 0.52 | 1                          | 0.94, 1.05        | 0.92        | 1.00                      | 0.96, 1.04 | 0.84 | 1.00                     | 0.97, 1.04 | 0.84 |
| GrimAgeAccel                                                                | 0.05                   | 0.20 | 0.02                | 0.62 | <b>1.08</b>                | <b>1.01, 1.16</b> | <b>0.03</b> | 0.99                      | 0.94, 1.05 | 0.80 | 1.01                     | 0.96, 1.06 | 0.69 |
| FitAgeAccel                                                                 | 0.00                   | 0.94 | 0.02                | 0.65 | 1.02                       | 0.96,1.10         | 0.49        | 1.02                      | 0.97, 1.07 | 0.51 | 0.99                     | 0.94, 1.04 | 0.69 |
| PACE                                                                        | -0.01                  | 0.80 | -0.05               | 0.17 | 8.8                        | 0.69,117.24       | 0.10        | 0.38                      | 0.05, 2.80 | 0.34 | 3.06                     | 0.48, 19.7 | 0.24 |
| PoAm                                                                        | 0.03                   | 0.35 | -0.03               | 0.34 | NA                         | NA                | NA          | 1.63                      | 0.09, 27.9 | 0.74 | 7.85                     | 0.56, 113  | 0.13 |
| Zhang MRS                                                                   | 0.00                   | 0.91 | -0.01               | 0.85 | 1.98                       | 0.86,4.60         | 0.11        | 1.19                      | 0.64, 2.22 | 0.58 | 0.88                     | 0.49, 1.58 | 0.68 |
| DNAmTL                                                                      | 0.10                   | 0.17 | -0.03               | 0.68 | 0.29                       | 0.05,1.49         | 0.14        | 0.31                      | 0.09, 1.02 | 0.05 | 1.31                     | 0.42, 4.10 | 0.65 |
| <b>Model 2 (adjusted for age, sex, lifestyle and blood cell proportion)</b> |                        |      |                     |      |                            |                   |             |                           |            |      |                          |            |      |
| IEAA                                                                        | 0.04                   | 0.16 | 0.01                | 0.75 | 0.96                       | 0.90, 1.03        | 0.28        | 0.96                      | 0.91, 1.01 | 0.11 | 0.99                     | 0.94, 1.04 | 0.63 |
| EEAA                                                                        | -0.02                  | 0.66 | 0.00                | 0.94 | 1.03                       | 0.96, 1.11        | 0.36        | 1.01                      | 0.96, 1.06 | 0.72 | 0.98                     | 0.93, 1.03 | 0.36 |
| Skin&BloodAgeAccel                                                          | 0.05                   | 0.08 | 0.03                | 0.43 | 0.93                       | 0.85, 1.03        | 0.16        | 0.99                      | 0.93, 1.06 | 0.74 | 0.99                     | 0.93, 1.06 | 0.81 |
| PhenoAgeAccel                                                               | 0.01                   | 0.70 | 0.03                | 0.43 | 1.00                       | 0.94, 1.06        | 0.96        | 1.00                      | 0.96, 1.04 | 0.92 | 1.00                     | 0.96, 1.04 | 0.94 |
| GrimAgeAccel                                                                | 0.04                   | 0.29 | -0.01               | 0.81 | 1.09                       | 1.00, 1.20        | 0.05        | 0.99                      | 0.93, 1.06 | 0.80 | 1.01                     | 0.95, 1.08 | 0.72 |
| FitAgeAccel                                                                 | 0.02                   | 0.55 | 0.01                | 0.79 | 1.02                       | 0.94, 1.11        | 0.66        | 1.01                      | 0.95, 1.07 | 0.83 | 0.97                     | 0.92, 1.03 | 0.28 |
| PACE                                                                        | -0.02                  | 0.50 | -0.06               | 0.12 | 9.45                       | 0.53, 181         | 0.13        | 0.45                      | 0.05, 4.07 | 0.48 | 3.88                     | 0.50, 30.4 | 0.19 |
| PoAm                                                                        | 0.01                   | 0.77 | -0.06               | 0.14 | NA                         | NA                | NA          | 2.27                      | 0.08, 68.8 | 0.64 | 21.2                     | 0.84, 573  | 0.07 |
| Zhang MRS                                                                   | -0.04                  | 0.40 | -0.07               | 0.24 | 3.14                       | 0.83, 12.3        | 0.10        | 1.45                      | 0.56, 3.74 | 0.44 | 0.63                     | 0.25, 1.55 | 0.31 |
| DNAmTL                                                                      | 0.05                   | 0.47 | -0.01               | 0.84 | 0.37                       | 0.06, 2.44        | 0.30        | 0.41                      | 0.11, 1.53 | 0.18 | 1.68                     | 0.48, 5.90 | 0.42 |

The analysis included selected epigenetic clocks, namely DNAm Age Horvath2013, DNAm Age Hannum, DNAm Age Skin & Blood and DNAmTL. Additionally, epigenetic age acceleration (EAA) measures were calculated as the residuals from regressing DNAm age on chronological age. EAA measures comprised intrinsic epigenetic age acceleration (IEAA), calculated using the Horvath2013 clock; extrinsic epigenetic age acceleration (EEAA), estimated using the Hannum clock; DNAm PhenoAge acceleration (PhenoAgeAccel); DNAm GrimAge acceleration (GrimAgeAccel); and DNAm FitAge acceleration (FitAgeAccel). Additionally, DNAm-based pace of aging metrics (PACE and PoAm) and the epigenetic mortality risk score (Zhang MRS) were included in the analysis.

Std. B: standardized beta coefficient from linear regression; OR: odds ratio from logistic regression; 95% CI: 95% confidence interval.

Model 2 for continuous traits:  $\text{lm}(\text{wrinkle}(\text{linear}) \sim \text{EAA} + \text{Age} + \text{Sex} + \text{Smoking} + \text{Stress} + \text{Skin color Fitzpatrick} + \text{Solarium} + \text{Frequency of tanning} + \text{CD8T} + \text{CD4T} + \text{NK} + \text{Bcell} + \text{Mono} + \text{Gran})$

Model 2 for binary traits:  $\text{glm}(\text{wrinkle}(\text{binary}) \sim \text{EAA} + \text{Age} + \text{Sex} + \text{Smoking} + \text{Stress} + \text{Skin color Fitzpatrick} + \text{Solarium} + \text{Frequency of tanning} + \text{CD8T} + \text{CD4T} + \text{NK} + \text{Bcell} + \text{Mono} + \text{Gran})$

Significant results are marked with bold

Facial height and lip height were measured on a continuous scale. Glogau photogaging: a two-stage categorization was used, comparing categories III and IV vs. categories I and II (reference); Nasolabial folds, eyelid drooping, full face wrinkles, forehead wrinkles, crow's feet, wrinkles over the lips: deep wrinkles vs. small wrinkles (reference) were analysed.

**Supplementary Table 11.** The list of the top GO terms for DMSs associated with different facial skin aging phenotypes at suggestive  $p < 1.0 \times 10^{-5}$ .

| Skin aging trait                     | Ontology | TERM                                                                    | Sig. Genes in Set                                                                                              | P.DE     |
|--------------------------------------|----------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|----------|
| Wrinkle area                         | CC       | apical part of cell                                                     | EDAR, NRG1, GNAT3                                                                                              | 0.0004   |
|                                      | BP       | positive regulation of peptidyl-tyrosine autophosphorylation            | NRG1                                                                                                           | 0.0007   |
|                                      | BP       | signaling                                                               | EDAR, RIMBP2, NRG1, GNAT3, WNT9A, DLGAP1, NFE2L3                                                               | 0.0008   |
|                                      | BP       | cell communication                                                      | EDAR, RIMBP2, NRG1, GNAT3, WNT9A, DLGAP1, NFE2L3                                                               | 0.0008   |
|                                      | BP       | regulation of peptidyl-tyrosine autophosphorylation                     | NRG1                                                                                                           | 0.001    |
|                                      | CC       | synapse                                                                 | AGAP1, RIMBP2, NRG1, DLGAP1                                                                                    | 0.001    |
|                                      | BP       | tube lumen cavitation                                                   | EDAR                                                                                                           | 0.001    |
|                                      | BP       | salivary gland cavitation                                               | EDAR                                                                                                           | 0.001    |
|                                      | BP       | ERBB2-ERBB4 signaling pathway                                           | NRG1                                                                                                           | 0.002    |
| Photonumeric full-face wrinkle score | MF       | ErbB-3 class receptor binding                                           | NRG1                                                                                                           | 0.002    |
|                                      | BP       | generation of neurons                                                   | CDH4, CNGB1, EML1, ZMYND8, GLI3, GLDN, NGF, ROR1, ATL1, LRRC7, BCL11B, SOX2, TBCD                              | 0.0002   |
|                                      | BP       | nervous system development                                              | CDH4, CNGB1, C1QL2, EML1, ZMYND8, SDCBP2, GLI3, GLDN, NGF, ROR1, ATL1, LRRC7, BCL11B, SIM1, SLC6A3, SOX2, TBCD | 0.0003   |
|                                      | BP       | neuron differentiation                                                  | CDH4, CNGB1, ZMYND8, GLI3, GLDN, NGF, ROR1, ATL1, LRRC7, BCL11B, SOX2, TBCD                                    | 0.0004   |
|                                      | BP       | adenohypophysis development                                             | SLC6A3, SOX2                                                                                                   | 0.0009   |
|                                      | BP       | thymocyte apoptotic process                                             | GLI3, BCL11B                                                                                                   | 0.002    |
|                                      | CC       | axon                                                                    | CNGB1, GLDN, NGF, ROR1, ATL1, LRRC7, SLC6A3                                                                    | 0.002    |
|                                      | BP       | regulation of neuron differentiation                                    | GLI3, NGF, BCL11B, SOX2                                                                                        | 0.002    |
|                                      | BP       | subpallium development                                                  | GLI3, BCL11B                                                                                                   | 0.002    |
|                                      | BP       | regulation of collagen binding                                          | GTPBP4                                                                                                         | 0.003    |
|                                      | BP       | negative regulation of collagen binding                                 | GTPBP4                                                                                                         | 0.003    |
| Lip wrinkles                         | BP       | spinal cord interneuron axon guidance                                   | EVX1, LHX9                                                                                                     | 6.95e-05 |
|                                      | BP       | interneuron axon guidance                                               | EVX1, LHX9                                                                                                     | 0.0001   |
|                                      | BP       | regulation of fermentation                                              | CAVIN3, ACTN3                                                                                                  | 0.0002   |
|                                      | BP       | membrane depolarization during SA node cell action potential            | HCN4, CACNA1D                                                                                                  | 0.0002   |
|                                      | BP       | fermentation                                                            | CAVIN3, ACTN3                                                                                                  | 0.0003   |
|                                      | BP       | negative regulation of feeding behavior                                 | MC4R, UCN                                                                                                      | 0.0003   |
|                                      | CC       | neuron projection                                                       | HCN4, EVX1, SIRT2, GABRA1, KCND2, KCNQ2, PCSK2, SYBU, CX3CL1, TULP1, UCN, CALCR, CAMK2A, ESPN, PSD2, RNF40     | 0.0004   |
|                                      | MF       | voltage-gated monoatomic cation channel activity                        | HCN4, KCND2, KCNQ2, CACNA1D, CACNB4                                                                            | 0.0005   |
|                                      | CC       | postsynaptic specialization                                             | DMTN, GABRA1, KCND2, RPL38, PRRT1, CAMK2A, DCLK1, DLGAP1                                                       | 0.0005   |
|                                      | BP       | peptidyl-threonine phosphorylation                                      | DMTN, SIRT2, HIPK2, CAMK2A                                                                                     | 0.0005   |
| Perceived facial age                 | MF       | RNA polymerase I cis-regulatory region sequence-specific DNA binding    | UBTF                                                                                                           | 0.002    |
|                                      | BP       | negative regulation of microtubule nucleation                           | ARHGEF7                                                                                                        | 0.003    |
|                                      | MF       | N-acetyllactosaminide beta-1,6-N-acetylglucosaminyltransferase activity | GCNT2                                                                                                          | 0.003    |
|                                      | MF       | POZ domain binding                                                      | KLHL17                                                                                                         | 0.003    |
|                                      | MF       | RNA polymerase I general transcription initiation factor activity       | UBTF                                                                                                           | 0.004    |
|                                      | BP       | zonula adherens assembly                                                | DLG5                                                                                                           | 0.005    |
|                                      | BP       | regulation protein catabolic process at postsynapse                     | KLHL17                                                                                                         | 0.006    |
|                                      | MF       | tRNA (guanine) methyltransferase activity                               | TARBP1                                                                                                         | 0.007    |
|                                      | BP       | regulation of smoothened signaling pathway                              | GAS1, DLG5                                                                                                     | 0.008    |
|                                      | MF       | insulin-like growth factor receptor activity                            | CRIM1                                                                                                          | 0.009    |

P.DE (P-value for over-representation of the GO term). ONTOLOGY: testing GO pathways. "BP" - biological process, "CC" - cellular component, "MF" - molecular function. Sig. Genes in Set: Significant differentially methylated genes overlapping with the gene set of interest.

**Supplementary Table 12.** Functional analysis of the genome-wide significant SNPs detected in GWAS.

| Skin aging trait     | chr | variant     | Genotype | Enhancer<br>histone marks | Motifs changed     | GENCODE<br>genes |
|----------------------|-----|-------------|----------|---------------------------|--------------------|------------------|
| Wrinkle Area         | 18  | rs73943403  | A>G      | ESC, BLD                  | Foxa, STAT, ZNF263 | RP11-78F17.1     |
|                      | 18  | rs79620305  | A>G      |                           | 4 altered motifs   | RP11-78F17.1     |
| Perceived Facial Age | 19  | rs74854711  | G>A      | SKIN, GI, MUS             | SMC3               | ZC3H4            |
|                      | 19  | rs113125564 | T>C      |                           | Eomes, Pax-4, Sox  | ZC3H4            |