## SUPPLEMENTARY TABLES

**Supplementary Table 1. 850K methylation information. Annotations were obtained using the BiocManager package in R.**

| 850K methylation array | | | | | | | |
|---|---|---|---|---|---|---|---|
| **CpG Name** | **Annotation** | **Position** | **Relation to Island** | **UCSC Ref Gene Name** | **UCSC Ref Gene Accession** | **UCSC Ref Gene Group** | **Regulatory Feature Group** |
| cg25053252 | chr17:7589290-7589503 | 7589358 | Island | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg17461511 | chr17:7591494-7591839 | 7591552 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| cg02045224 | chr17:7591494-7591839 | 7591618 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| cg07991600 | chr17:7589290-7589503 | 7589380 | Island | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg02087342 | NA | 7579047 | Open Sea | ***TP53*** | NM_000546 | Body | |
| cg22949073 | NA | 7572391 | Open Sea | ***TP53*** | NM_000546 | 3′UTR | |
| cg13169780 | chr17:7591494-7591839 | 7591570 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| cg07760161 | chr17:7589290-7589503 | 7588378 | N Shore | ***TP53*** | NM_000546 | 5′UTR | PA; CTS |
| cg02166782 | chr17:7591494-7591839 | 7591564 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| cg22175811 | chr17:7591494-7591839 | 7590052 | N Shore | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg21050342 | chr17:7591494-7591839 | 7591644 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| cg13468400 | NA | 7579546 | Open Sea | ***TP53*** | NM_000546 | Body | |
| cg08119584 | chr17:7591494-7591839 | 7589976 | N Shore | ***TP53*** | NM_000546 | 5′UTR | PA |
| **cg18198734** | **NA** | **7579263** | **Open Sea** | ***TP53*** | **NM_000546** | **Body** | |
| cg23290969 | chr17:7589290-7589503 | 7589272 | N Shore | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg16397722 | NA | 7577090 | Open Sea | ***TP53*** | NM_000546 | Body | |
| cg12041075 | NA | 7579312 | Open Sea | ***TP53*** | NM_000546 | Body | |
| cg08691422 | chr17:7589290-7589503 | 7588787 | N Shore | ***TP53*** | NM_000546 | 5′UTR | |
| cg15206330 | chr17:7591494-7591839 | 7591591 | Island | ***TP53*** | NM_000546 | TSS1500 | PA |
| **cg12041429** | **chr17:7589290-7589503** | **7585875** | **N Shelf** | ***TP53*** | **NM_000546** | **5′UTR** | |
| cg02842899 | chr17:7589290-7589503 | 7589491 | Island | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg01620719 | chr17:7589290-7589503 | 7589251 | N Shore | ***TP53*** | NM_000546 | 5′UTR | PA |
| cg10792831 | NA | 7578689 | Open Sea | ***TP53*** | NM_000546 | Body | |
| cg06365412 | NA | 7580709 | Open Sea | ***TP53*** | NM_000546 | 5′UTR | |
| cg27182172 | chr4:23890120-23890955 | 23890890 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg09082664 | chr4:23499647-23499989 | 23890701 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg27514608 | chr4:23892305-23892675 | 23892540 | Open Sea | ***PGC1A*** | NM_013261 | TSS1500 | |
| cg05158538 | chr4:23891440-23891870 | 23891486 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg10955995 | chr4:23857865-23858250 | 23858146 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg27461259 | chr4:23892305-23892675 | 23892621 | Open Sea | ***PGC1A*** | NM_013261 | TSS1500 | |
| cg07744449 | NA | 23887314 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg08550435 | chr4:23829600-23829910 | 23829879 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg02896941 | chr4:23499647-23499989 | 23890659 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg19701879 | chr4:23880820-23881155 | 23881105 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg11270806 | chr4:23892305-23892675 | 23892515 | Open Sea | ***PGC1A*** | NM_013261 | TSS1500 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| cg24716152 | chr4:23879168-23881165 | 23879965 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg12691631 | chr4:23891440-23891870 | 23891835 | Open Sea | ***PGC1A*** | NM_013261 | TSS200 | |
| cg15541091 | chr4:23812780-23813175 | 23813125 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg06772578 | NA | 23796624 | Open Sea | ***PGC1A*** | NM_013261 | 3′UTR | |
| cg09427718 | chr4:23819243-23820433 | 23819929 | Open Sea | ***PGC1A*** | NM_013261 | Body | |
| cg20723350 | chr4:23891440-23891870 | 23891596 | Open Sea | ***PGC1A*** | NM_013261; NM_013261 | 1stExon; 5′UTR | |
| cg10582690 | chr10:69644169-69645178 | 69644422 | Island | ***SIRT1*** | NM_012238 | TSS200 | PA |
| cg07832903 | chr10:69644169-69645178 | 69644926 | Island | ***SIRT1*** | NM_012238 | Body | PA |
| cg00972288 | chr10:69644169-69645178 | 69644348 | Island | ***SIRT1*** | NM_012238 | TSS200 | PA |
| cg19681528 | chr10:69644169-69645178 | 69644405 | Island | ***SIRT1*** | NM_012238 | TSS200 | PA |
| cg02720207 | chr10:69644169-69645178 | 69644399 | Island | ***SIRT1*** | NM_012238 | TSS200 | PA |
| cg25513531 | chr10:69644169-69645178 | 69644407 | Island | ***SIRT1*** | NM_012238 | TSS200 | PA |
| cg26075202 | chr10:69644169-69645178 | 69645177 | Island | ***SIRT1*** | NM_012238 | Body | |
| cg10705386 | chr10:69644169-69645178 | 69644512 | Island | ***SIRT1*** | NM_012238 | 1stExon | PA |
| cg01128800 | chr10:69644169-69645178 | 69644938 | Island | ***SIRT1*** | NM_012238 | Body | PA |
| cg00851987 | chr10:69662340-69664884 | 69664037 | Open Sea | ***SIRT1*** | NM_012238 | Body | |
| cg03251249 | chr10:69644169-69645178 | 69645012 | Island | ***SIRT1*** | NM_012238 | Body | PA |
| cg05506809 | chr10:69644169-69645178 | 69648299 | S Shelf | ***SIRT1*** | NM_012238 | Body | |
| cg19192316 | chr10:69644169-69645178 | 69643020 | N Shore | ***SIRT1*** | NM_012238 | TSS1500 | |
| cg23988827 | NA | 69676715 | Open Sea | ***SIRT1*** | NM_012238 | 3'UTR | |
| cg19980381 | chr10:69644169-69645178 | 69644128 | N Shore | ***SIRT1*** | NM_012238 | TSS1500 | PA |
| cg13796676 | chr10:69644169-69645178 | 69648687 | S Shelf | ***SIRT1*** | NM_012238 | Body | |

Abbreviations: NA: not applicable; PA: Promotor Associated; CTS: Cell Type Specific.

**Supplementary Table 2. Rotated loadings. Bold loadings have an absolute value larger than 0.45, meaning the CpG is selected as relevant for the specific PC.**

| | | | ***TP53*** | | |
|---|---|---|---|---|---|
| **CpG** | **PC1** | **PC2** | **PC3** | **PC4** | **PC5** |
| cg01620719 | –0.11 | 0.16 | 0.35 | 0.02 | 0.44 |
| cg02045224 | –0.20 | 0.27 | –0.07 | 0.17 | –0.16 |
| cg02087342 | **0.55** | 0.27 | 0.06 | –0.08 | –0.16 |
| cg02166782 | –0.01 | 0.32 | 0.31 | 0.27 | –0.26 |
| cg02842899 | –0.12 | **0.47** | –0.05 | 0.04 | –0.35 |
| cg06365412 | 0.37 | 0.36 | –0.27 | –0.06 | 0.42 |
| cg07760161 | –0.01 | 0.18 | **0.60** | –0.25 | 0.25 |
| cg07991600 | **–0.56** | 0.26 | –0.22 | 0.20 | 0.32 |
| cg08119584 | 0.03 | 0.16 | 0.18 | 0.34 | –0.23 |
| cg08691422 | 0.04 | 0.21 | **0.58** | –0.16 | 0.04 |
| cg10792831 | **0.49** | 0.42 | 0.14 | –0.32 | 0.03 |
| cg12041075 | 0.43 | **0.46** | –0.24 | –0.15 | 0.09 |
| cg12041429 | **0.72** | –0.25 | –0.02 | 0.24 | 0.09 |
| cg13169780 | 0.04 | 0.14 | 0.04 | 0.26 | 0.03 |
| cg13468400 | –0.04 | 0.32 | 0.04 | –0.44 | –0.36 |

| | | | | | |
|---|---|---|---|---|---|
| cg15206330 | –0.07 | 0.23 | 0.36 | 0.20 | –0.03 |
| cg16397722 | **0.54** | –0.21 | 0.17 | 0.00 | 0.03 |
| cg17461511 | –0.42 | 0.44 | –0.25 | –0.15 | 0.13 |
| cg18198734 | 0.35 | **0.61** | –0.25 | –0.06 | –0.21 |
| cg21050342 | 0.05 | 0.25 | 0.31 | **0.47** | 0.25 |
| cg22175811 | –0.17 | 0.17 | 0.38 | –0.06 | 0.33 |
| cg22949073 | **0.64** | –0.10 | –0.05 | 0.34 | 0.07 |
| cg23290969 | –0.03 | 0.20 | 0.22 | 0.00 | –0.40 |
| cg25053252 | **–0.62** | 0.29 | –0.19 | 0.10 | –0.01 |

***PGC1A***

| CpG | PC1 | PC2 | PC3 | PC4 | PC5 |
|---|---|---|---|---|---|
| cg02896941 | 0.04 | 0.06 | 0.02 | –0.07 | 0.02 |
| cg05158538 | 0.08 | 0.07 | –0.09 | –0.10 | –0.06 |
| cg06772578 | 0.30 | 0.21 | 0.21 | –0.12 | –0.07 |
| cg07744449 | 0.20 | 0.19 | 0.19 | –0.09 | –0.09 |
| cg08550435 | **0.45** | 0.05 | 0.10 | –0.08 | –0.11 |
| cg09082664 | –0.04 | –0.14 | –0.14 | 0.07 | –0.11 |
| cg09427718 | **0.54** | –0.05 | 0.10 | 0.06 | 0.08 |
| cg10955995 | 0.20 | –0.02 | 0.10 | 0.08 | 0.05 |
| cg11270806 | 0.04 | –0.02 | –0.05 | –0.08 | 0.04 |
| cg12691631 | 0.06 | 0.03 | –0.02 | 0.04 | –0.16 |
| cg15541091 | 0.20 | 0.32 | 0.20 | –0.11 | –0.19 |
| cg19701879 | **0.48** | –0.13 | –0.14 | 0.06 | –0.02 |
| cg20723350 | 0.05 | 0.03 | 0.00 | 0.02 | –0.09 |
| cg24716152 | 0.29 | –0.26 | –0.22 | 0.14 | 0.02 |
| cg27182172 | –0.02 | –0.07 | –0.09 | –0.01 | 0.03 |
| cg27461259 | 0.04 | 0.12 | 0.01 | –0.01 | 0.03 |
| cg27514608 | 0.20 | –0.11 | –0.01 | 0.00 | –0.08 |

***SIRT1***

| CpG | PC1 | PC2 | PC3 | PC4 | PC5 |
|---|---|---|---|---|---|
| cg00851987 | **–0.51** | 0.14 | –0.10 | –0.15 | 0.28 |
| cg00972288 | –0.01 | 0.28 | –0.08 | **0.68** | –0.22 |
| cg01128800 | **0.69** | **0.45** | –0.32 | –0.08 | –0.16 |
| cg02720207 | **0.49** | 0.40 | 0.18 | –0.17 | 0.04 |
| cg03251249 | 0.00 | –0.03 | –0.22 | **0.59** | **0.48** |
| cg05506809 | **–0.56** | **0.60** | –0.12 | 0.13 | –0.06 |
| cg07832903 | 0.01 | 0.00 | **0.55** | 0.27 | **–0.62** |
| cg10582690 | **0.73** | 0.34 | –0.15 | –0.21 | –0.16 |
| cg10705386 | 0.41 | 0.36 | 0.19 | 0.02 | 0.11 |
| cg13796676 | **–0.66** | **0.57** | –0.05 | 0.21 | –0.01 |
| cg19192316 | **–0.65** | 0.18 | 0.03 | –0.07 | 0.25 |
| cg19681528 | 0.35 | 0.23 | 0.25 | –0.24 | –0.08 |
| cg19980381 | –0.02 | 0.05 | **0.64** | 0.03 | 0.28 |
| cg23988827 | **–0.46** | **0.61** | –0.17 | –0.09 | –0.13 |
| cg25513531 | 0.08 | 0.35 | 0.42 | 0.11 | 0.03 |
| cg26075202 | **0.76** | 0.31 | –0.27 | –0.21 | –0.14 |

**Supplementary Table 3. Comparison of the characteristics between our study population (*n* = 613) and full ENVIR*ON*AGE data (*n* = 1530).**

| Characteristic | Analyzed population Mean ± SD or *n* (%) (*n* = 613) | Total population Mean ± SD or *n* (%) (*n* = 1530) | *P*-value |
|---|---|---|---|
| **Mothers** | | | |
| Age, y | 29.3 ± 4.6 | 29.4 ± 4.55 | 0.64 |
| Pre-pregnancy BMI, kg/m$^2$ | 24.6 ± 4.8 | 24.5 ± 4.76 | 0.66 |
| Educational level | | | |
| Low | 79 (12.9%) | 160 (10.5%) | 0.13 |
| Middle | 227 (37.0%) | 500 (32.7%) | 0.064 |
| High | 307 (50.1%) | 726 (47.5%) | 0.32 |
| Smoking status | | | |
| Never smoker | 391 (63.8%) | 897 (58.6%) | 0.030 |
| Former smoker | 154 (25.1%) | 326 (21.3%) | 0.064 |
| Current smoker | 68 (11.1%) | 173 (11.3%) | 0.95 |
| Parity | | | |
| 1 | 337 (55.0%) | 751 (49.1%) | 0.015 |
| 2 | 206 (33.6%) | 507 (33.1%) | 0.86 |
| ≥ | 70 (11.4%) | 172 (11.2%) | 0.95 |
| **Newborns** | | | |
| Sex | | | |
| Female | 321 (52.4%) | 736 (48.1%) | 0.10 |
| Gestational age, wk | 39.2 ± 1.7 | 39.2 ± 1.6 | 0.91 |
| Birth weight, g | 3420 ± 496 | 3400 ± 495 | 0.52 |
| Ethnicity | | | |
| European-Caucasian | 533 (86.9%) | 1221 (79.8%) | 0.0001 |
| Season of birth | | | |
| Winter | 150 (24.5%) | 372 (24.3%) | 0.97 |
| Spring | 149 (24.3%) | 344 (22.5%) | 0.40 |
| Summer | 151 (24.6%) | 329 (21.5%) | 0.13 |
| Autumn | 163 (26.6%) | 385 (25.2%) | 0.54 |

**Supplementary Table 4. Association between mitochondrial DNA content (mtDNAc) and cord plasma protein levels (p53 and PGC-1α) and between the cord plasma protein levels.**

| | Cord p53 (*n* = 613) | | Cord PGC-1α (*n* = 607) | |
|---|---|---|---|---|
| | % difference (95% CI) | *P*-value | % difference (95% CI) | *P*-value |
| **Cord mtDNAc** | –0.0082 (–0.51, 0.50) | 0.99 | 0.27 (–0.91, 1.47) | 0.26 |
| **Placenta mtDNAc*** | –0.30 (–0.86, 0.27) | 0.31 | –0.74 (–2.05, 0.58) | 0.27 |
| **Cord PGC-1α** | 0.12 (–0.21, 0.44) | 0.51 | NA | NA |

Estimates are presented as percentage difference with 95% CI for a 10% change in explanatory variable. All models are adjusted for technical covariates (sample storage and batch effects), newborn's sex, gestational age, maternal BMI, maternal and paternal age, ethnicity, parity, smoke status, maternal education and month of delivery. Cord plasma p53 and PGC-1α represent the exposure variable, while the variables in the left column represent the outcome variable. *Data available for *n* = 575. Abbreviation: NA: not applicable.

**Supplementary Table 5. Association between Principle Components (PCs) of *TP53*, *PGC1A* and *SIRT1* methylation levels and cord blood telomere length, cord blood mitochondrial DNA content (mtDNAc) and cord plasma protein levels (p53 and PGC-1α).**

| | Cord TL (*n* = 200) | Cord mtDNA (*n* = 205) | Cord p53 (*n* = 205) | Cord PGC-1α (*n* = 205) |
|---|---|---|---|---|
| | % difference (95% CI) | % difference (95% CI) | % difference (95% CI) | % difference (95% CI) |
| ***TP53*** | | | | |
| PC1 | −1.00 (−2.48, 0.50) | −0.48 (−4.43, 3.63) | **−5.58 (−1.25, −0.66)** | 0.27 (−2.72, 3.35) |
| PC2 | **1.74 (−0.073, 3.58)** | 0.32 (−4.51, 5.39) | **−4.63 (−9.79, 0.83)** | −1.00 (−4.55, 2.68) |
| PC3 | −1.38 (−3.36, 0.65) | −0.11 (−5.62, 5.71) | −3.23 (−9.73, 3.74) | 0.13 (−3.90, 4.33) |
| PC4 | **−2.46 (−4.84, -0.024)** | −2.96 (−9.28, 3.81) | −4.63 (−12.42, 3.85) | −0.20 (−5.10, 4.96) |
| PC5 | −0.63 (−2.84, 1.64) | **−10.52 (−15.59,-5.14)** | 2.59 (−5.16, 10.96) | 0.77 (−3.79, 5.54) |
| ***PGC1A*** | | | | |
| PC1 | −0.31 (−1.88, 1.29) | −0.17 (4.06, 3.89) | −2.51 (7.33, 2.55) | 1.15 (−1.82, 4.22) |
| PC2 | −0.65 (-2.47, 1.21) | −0.34 (−5.24, 4.81) | −1.39 (−7.30, 4.89) | −0.26 (−3.82, 3.44) |
| PC3 | **2.20 (0.11, 4.34)** | 4.47 (−0.92, 10.78) | −0.18 (−7.08, 7.024) | −0.77 (−4.87, 3.52) |
| PC4 | −0.77 (-2.99, 1.50) | 2.50 (−3.38, 8.74) | −3.87 (−11.09, 3.93) | 0.98 (−3.57, 5.74) |
| PC5 | 0.91 (-1.66, 3.54) | −3.98 (−10.38, 2.88) | 3.58 (−5.27, 13.25) | 2.71 (−2.55, 8.25) |
| ***SIRT1*** | | | | |
| PC1 | 0.12 (-1.27, 1.52) | −2.43 (−5.96, 1.32) | 0.73 (−3.80, 5.47) | −0.26 (−2.93, 2.48) |
| PC2 | −0.41 (-2.25, 1.46) | **−4.15 (−8.42, 0.80)** | −0.76 (−6.84, 5.72) | −0.79 (−4.42, 2.97) |
| PC3 | 1.00 (-1.31, 3.37) | −1.18 (−6.97, 4.96) | −3.23 (−10.66, 4.81) | −2.57 (−7.04, 2.12) |
| PC4 | 0.52 (-1.99, 3.08) | 4.20 (−2.30, 11.14) | 0.48 (−7.79, 9.48) | 4.41 (−0.70, 9.78) |
| PC5 | 1.10 (-1.63, 3.91) | 0.11 (−6.92, 7.67) | −5.28 (−13.83, 4.12) | −0.77 (−6.16, 4.94) |

Estimates are presented as percentage difference with 95% CI for a one-unit change in exposure variable. All models are adjusted for technical covariates (sample storage and batch effects), newborn's sex, gestational age, maternal BMI, maternal and paternal age, ethnicity, parity, smoke status, maternal education and month of delivery. The variables in columns represent the response variables, while the variables in the rows represent the explanatory variables. Bold values indicate significant estimates.