

SUPPLEMENTARY TABLES

Supplementary Table 1. The summary of the pairwise Pearson correlations of the CpGs which passed pre-screening by an epigenome-wide association analysis.

	min	5th percentile	Median	95th percentile	max
Cord blood telomere length ¹	-0.95	-0.19	0.05	0.78	0.99
Telomere attrition rate ²	-0.96	-0.28	0.03	0.49	0.98

¹260,296,336 pairwise Pearson correlations of 22,817 CpGs.

²48,624,591 pairwise Pearson correlations of 9,862 CpGs.

Supplementary Table 2. The 47 CpGs and 7 interactions in the model of baseline telomere length.

Name of CpG or interaction	Coefficient (bootstrap p-value)	EWAS Coefficient (p-value)	Chromosome	Position on chromosome	Relation to island	Gene name	DMR	Promoter associated
(intercept)	1.1605 (0.00e+00)							
cg00036011	0.0169 (4.00e-04)	20.68 (9.17e-04)	chr6	26271718	N_Shore	HIST1H3G; HIST1H2BI		
cg00064950	-0.0135 (1.10e-03)	-8.51 (4.32e-03)	chr17	7184216	Island	SLC2A4		
cg00487989	0.0177 (7.00e-04)	7.64 (7.07e-04)	chr16	89688244	OpenSea	DPEP1		
cg00871560	0.0112 (1.12e-02)	1.47 (2.32e-04)	chr3	132756721	N_Shore	TMEM108		
cg00973724	0.0109 (1.18e-02)	7.43 (2.76e-03)	chr12	49524797	Island	TUBA1B		yes
cg00973724:cg00064950	-0.0086 (2.66e-02)					<i>TUBA1B * SLC2A4</i>		
cg01567315	0.0156 (1.10e-03)	4.52 (2.60e-04)	chr1	155650264	OpenSea	YY1AP1		
cg02576753	0.0132 (4.40e-03)	1.56 (2.56e-06)	chr15	27772640	OpenSea	GABRG3		
cg02802645	-0.0139 (5.60e-03)	-6.17 (3.64e-03)	chr22	38904757	S_Shore			
cg03891344	-0.0193 (4.00e-04)	-9.98 (1.25e-04)	chr16	19533212	Island	GDE1		yes
cg04372430	-0.0074 (7.54e-02)	-9.06 (6.31e-03)	chr8	48591406	OpenSea	SPIDR		
cg04372430:cg16435922	-0.0171 (2.00e-04)							
cg06105699	0.0162 (4.00e-04)	1.15 (2.53e-03)	chr17	79971436	OpenSea	ASPSCR1		
cg06529600	-0.0066 (1.18e-01)	-2.15 (2.60e-03)	chr6	112652308	OpenSea			
cg06826039	-0.0099 (2.82e-02)	-6.65 (3.07e-04)	chr1	204379650	N_Shore	PPP1R15B		yes
cg07131116	0.0113 (2.57e-02)	9.4 (2.34e-06)	chr14	94546722	N_Shore	DDX24; IFI27L1		yes
cg07417551	0.0108 (1.75e-02)	3.34 (3.30e-03)	chr19	14586295	S_Shore	PTGER1		
cg08878914	-0.0099 (2.53e-02)	-5.9 (4.85e-03)	chr8	86435445	OpenSea			
cg09793256	-0.0112 (9.80e-03)	-7.08 (4.66e-04)	chr2	55646604	N_Shore	CCDC88A	DMR	yes
cg09880724	-0.0142 (1.30e-03)	-34.01 (3.75e-03)	chr16	87425644	Island	FBXO31; MAP1LC3B		yes
cg11300971	0.0143 (4.10e-03)	1.88 (1.33e-04)	chr4	89619038	OpenSea	NAP1L5; HERC3		yes
cg11455582	-0.0129 (3.90e-03)	-8.57 (7.86e-03)	chr3	155272990	OpenSea	PLCH1		
cg12581244	0.0091 (6.35e-02)	4.65 (2.06e-03)	chr17	33700295	N_Shore	SLFN11		yes
cg13074173	-0.0074 (7.85e-02)	-3.27 (4.55e-03)	chr8	144462007	Island	RHPN1		
cg13074173:cg00973724	-0.0146 (2.20e-03)					<i>RHPN1 * TUBA1B</i>		
cg14055864	-0.0129 (7.50e-03)	-7.72 (3.72e-03)	chr3	138067120	Island	MRAS		
cg14102251	0.0062 (1.46e-01)	6.08 (7.67e-03)	chr14	75745098	Island	FOS		
cg14102251:cg12581244	0.0101 (2.70e-02)					<i>FOS * SLFN11</i>		
cg14264119	0.0169 (0.00e+00)	2.37 (5.41e-05)	chr10	11783794	N_Shore	ECHDC3		
cg14493336	0.0085 (3.73e-02)	0.68 (5.11e-03)	chr2	65295115	OpenSea	CEP68		
cg14493336:cg14264119	0.0091 (1.50e-02)					<i>CEP68 * ECHDC3</i>		
cg15380694	0.0125 (1.06e-02)	9.52 (3.49e-04)	chr8	125577065	OpenSea	MTSS1		yes
cg15661580	-0.0132 (6.00e-03)	-3.82 (1.04e-03)	chr10	71896835	OpenSea			
cg15821589	-0.0169 (2.00e-04)	-2.89 (8.26e-06)	chr1	78444904	Island	FUBP1		
cg16435922	0.016 (6.00e-04)	3.84 (4.55e-05)	chr16	55053053	Island			
cg17282982	0.0161 (0.00e+00)	34.56 (4.40e-05)	chr1	114355064	Island	RSBN1		yes
cg17332573	0.0126 (3.10e-03)	10.68 (1.22e-06)	chr6	26250934	N_Shore	HIST1H2BH; IST1H3F		yes
cg19822755	-0.0108 (7.60e-03)	-1.95 (1.97e-04)	chr16	30108259	S_Shore	YPEL3		
cg20249169	0.0128 (6.60e-03)	10.23 (2.72e-03)	chr2	64881356	Island	SERTAD2		

cg20249169:cg07417551	0.0191 (1.00e-03)					<i>SERTAD2 * PTGER1</i>		
cg20467667	0.0127 (6.10e-03)	15.65 (1.32e-06)	chr10	75987922	OpenSea	ADK		yes
cg21954346	0.0126 (5.80e-03)	8.03 (2.26e-04)	chr16	68271489	Island	ESRP2		yes
cg22069262	-0.0095 (4.73e-02)	-3.66 (6.60e-03)	chr7	1587402	Island	TMEM184A		
cg22335713	0.0106 (1.36e-02)	4.78 (3.94e-04)	chr10	123357603	Island	FGFR2		
cg22335713:cg22577984	-0.0157 (5.10e-03)					<i>FGFR2 * C2CD2L</i>		
cg22577984	-0.011 (1.83e-02)	-2.86 (5.99e-03)	chr11	118981363	S_Shelf	C2CD2L		
cg22749642	0.012 (4.70e-03)	1.29 (6.78e-03)	chr11	857033	N_Shore	TSPAN4		
cg23455212	-0.0056 (2.24e-01)	-1.7 (8.00e-03)	chr12	91505417	OpenSea	LUM		
cg24803876	0.0112 (1.07e-02)	12.81 (7.11e-04)	chr8	67340974	Island	RRS1		
cg26035817	-0.0115 (1.70e-02)	-1.89 (7.30e-04)	chr1	114414802	OpenSea	PTPN22		yes
cg26110653	-0.0139 (3.00e-04)	-6.7 (7.53e-06)	chr13	38924412	Island	UFM1		yes
cg26725552	-0.0143 (2.40e-03)	-2.77 (1.73e-03)	chr10	126314758	OpenSea	FAM53B		
cg26795934	0.0079 (1.01e-01)	23.3 (7.15e-06)	chr11	58421700	OpenSea			
ch.7.1140112F	0.0105 (3.39e-02)	10.2 (1.28e-05)	chr7	49032475	OpenSea			

From left to right column: names of the CpGs or CpG-CpG interactions, coefficients (contributing weights) of each CpG in the final model with bootstrap p-value, the fully adjusted association and corrected p-value obtained in epigenome-wide association analysis (EWAS), the chromosome where the CpGs were located and the genes to which the CpGs were mapped. Gene names of interaction terms (two gene names in italic and separated by “*”) indicate that both interacting CpGs were annotated with gene names.

Supplementary Table 3. The 31 CpGs and 5 interactions in the model of telomere attrition rate.

Name of CpG or interaction	Coefficient (bootstrap p-value)	EWAS Coefficient (p-value)	Chromosome	Position on chromosome	Relation to island	Gene name	DMR	Promoter associated
(intercept)	8e-04 (4.62e-01)							
cg02537587	0.002 (1.90e-03)	1.24 (3.32e-05)	chr12	3982809	S_Shore	PARP11		yes
cg02690648	0.0024 (1.00e-04)	1.93 (1.49e-06)	chr8	10683044	OpenSea	PINX1; MIR1322		
cg04043642	-0.0024 (4.00e-04)	-0.17 (6.00e-03)	chr20	55842871	S_Shore	BMP7		
cg04935434	0.0021 (2.10e-03)	1.12 (3.83e-03)	chr2	177024947	Island			
cg05201958	0.002 (7.00e-04)	0.14 (1.34e-03)	chr10	61968731	OpenSea	ANK3		
cg06107116	0.0019 (1.00e-03)	1.31 (6.96e-05)	chr6	33267515	Island	TAPBP; RGL2		yes
cg08134068	-0.0022 (3.00e-04)	-1.37 (9.09e-03)	chr7	151039078	Island	NUB1		yes
cg09366730	-0.0021 (1.90e-03)	-0.2 (4.61e-06)	chr4	2341370	Island	ZFYVE28		
cg10020325	0.0016 (9.90e-03)	0.17 (7.77e-03)	chr2	220362163	Island	GMPPA		yes
cg10020325:cg16798728	-0.0025 (1.00e-04)					<i>GMPPA * DPP6</i>		
cg11086312	0.002 (1.60e-03)	0.1 (9.34e-04)	chr14	92720273	OpenSea			
cg11872375	0.0024 (3.00e-04)	0.7 (3.43e-04)	chr12	124709358	OpenSea	ZNF664-FAM101A		
cg12267637	0.0018 (2.90e-03)	0.15 (7.96e-04)	chr2	4102455	OpenSea			
cg12267637:cg23423086	-0.0017 (4.20e-03)							
cg12782249	-0.0017 (4.50e-03)	-0.07 (6.00e-04)	chr15	91458455	OpenSea	MAN2A2		
cg13960352	0.0017 (3.10e-03)	0.59 (4.79e-06)	chr19	45826863	Island	CKM		
cg15072796	0.0015 (1.40e-02)	1.31 (9.86e-04)	chr10	105727772	S_Shore	SLK		
cg16467775	-0.0017 (4.30e-03)	-0.2 (7.31e-04)	chr16	90085110	Island	DBNDD1		
cg16718624	-0.0016 (3.70e-03)	-3.55 (1.38e-03)	chr3	77089518	S_Shore	ROBO2		
cg16798728	-0.0015 (7.50e-03)	-0.22 (7.03e-03)	chr7	153984755	OpenSea	DPP6		
cg16798728:cg15072796	-0.0022 (3.00e-04)					<i>DPP6 * SLK</i>		
cg16975599	0.0017 (7.40e-03)	0.15 (4.88e-05)	chr3	158962761	OpenSea	IQCJ		
cg17751153	-0.0021 (1.00e-03)	-0.39 (3.51e-04)	chr5	447880	OpenSea	EXOC3		yes
cg19027504	0.0025 (0.00e+00)	1.23 (1.39e-04)	chr12	40013700	OpenSea	ABCD2		yes
cg19291087	0.002 (1.00e-03)	1.27 (1.67e-04)	chr2	3502760	N_Shore	ADI1		
cg19291087:cg04935434	-0.0022 (4.00e-04)							
cg19291087:cg16718624	0.0021 (5.00e-04)					<i>ADI1 * ROBO2</i>		
cg19887293	-0.0015 (8.80e-03)	-0.2 (1.19e-03)	chr6	33132693	S_Shelf	COL11A2		
cg20054536	-0.0027 (7.00e-04)	-0.27 (1.40e-05)	chr19	376069	Island	THEG		

cg23155965	0.0021 (5.00e-04)	0.11 (2.70e-03)	chr10	134778176	N_Shore		
cg23423086	0.0017 (6.50e-03)	0.58 (1.24e-03)	chr11	85856245	OpenSea		
cg23965459	-0.0025 (0.00e+00)	-0.52 (3.71e-04)	chr14	104647094	S_Shore	<i>KIF26A</i>	
cg24101053	0.0021 (1.00e-03)	0.56 (1.03e-03)	chr5	14419738	OpenSea	<i>TRIO</i>	
cg24790788	-0.0015 (8.60e-03)	-0.1 (1.05e-03)	chr3	145879626	S_Shore	<i>PLOD2</i>	<i>RDMR</i>
cg24942922	-8e-04 (1.28e-01)	-0.17 (2.41e-04)	chr3	120003547	N_Shore		
cg25615010	0.0013 (3.78e-02)	1.9 (7.57e-03)	chr7	152456741	Island	<i>ACTR3B</i>	yes

From left to right column: names of the CpGs or CpG-CpG interactions, coefficients (contributing weights) of each CpG in the final model with bootstrap p-value, the fully adjusted association and corrected p-value obtained in epigenome-wide association analysis (EWAS), the chromosome where the CpGs were located and the genes to which the CpGs were mapped. DMR: differentially methylated region. RDMR: reprogramming-specific DMR. Gene names of interaction terms (two gene names in italic and separated by “*”) indicate that both interacting CpGs were annotated with gene names.

Supplementary Table 4. Comparison of characteristics of the selected with the total data in ENVIRONAGE cohort.

		Selected data (N=247)	Total data (N=916)
Newborns			
<i>Sex</i>	Female	121 (49.0%)	459 (50.1%)
<i>Ethnicity</i>	European	231 (93.5%)	808 (88.2%)
<i>Birth weight (kg)</i>		3.39 ± 0.44	3.39 ± 0.48
<i>Gestational age (weeks)</i>		39.24 ± 1.37	39.13 ± 1.58
Mothers			
<i>Education</i>	No diploma	24 (9.7%)	115 (12.6%)
	High school diploma	67 (27.1%)	333 (36.4%)
	A 3-year college	124 (50.2%)	354 (38.6%)
	A 4-year college or university	32 (13.0%)	114 (12.4%)
<i>Smoking status</i>	Never smoker	167(67.6%)	582 (63.5%)
	Former smoker	48 (19.4%)	210 (22.9%)
	Smoker	32 (13.0%)	124 (13.5%)
<i>Parity</i>	Primiparous	129 (52.2%)	503 (54.9%)
	Secundiparous	95 (38.5%)	313 (34.2%)
	Multiparous	23 (9.3%)	100 (10.9%)
<i>With pregnancy complications</i>		37 (15.0%)	166 (18.1%)
<i>Age at delivery (years)</i>		30.21 ± 4.38	29.29 ± 4.59
<i>Pre-pregnancy BMI (kg/m²)</i>		24.28 ± 4.56	24.26 ± 4.54
Fathers			
<i>Age at the mother’s delivery (years)</i>		32.87 ± 5.60	31.88 ± 5.52