

Supplementary information

-Decoupling of DNA methylation status and gene expression levels in aging individuals-

Table S1: Dataset Information

Datasets	Type	Total number of subjects	Age groups	Tissue	Paper	Source (doi)
Gene expression	Differential expressed genes	128	20-55, n= 55; 90-104, n=73	Whole blood	Häsler 2017	10.1111/ace1.12598
DNA methylation	Methylation values of >450K CpG sites	656	19-45, n= 68; 45-55, n= 123; 55-65, n= 174; 65-75, n= 168; 75-85, n= 134; 85-101, n= 53 (self-defined)	Whole blood	Hannum 2013	10.1016/j.molcel.2012.10.016

Table S2: Information about the different subsets; including total gene number and number of genes with detected CpG sites in CGIs in promoter region.

Subset	Total number of Genes	Genes with detected CGI
Whole Genome	28.456	12.774
All DEGs	Up: 1345, Down: 1743	Up: 848, Down: 1038
Most significant DEGs	Up: 25, Down: 25	Up: 15, Down: 16

Table S3: Output of statistical and linear regression analysis of the different groups of genes; including mean, coefficient, R²- and p-value.

Subsets	Mean	Coefficient	R ²	p-value
25 upregulated genes	0.1122389	4.3417E-05	0.02737276	2.055E-05
25 downregulated genes	0.06939925	5.6911E-05	0.0409773	1.704E-07
all upregulated genes	0.08138031	4.34E-05	0.02737506	2.05E-05
all downregulated genes	0.07255323	5.83E-05	0.04298734	8.39E-08
whole genome	0.1127094	9.18E-05	0.05960493	2.34E-10

Table S4: Summary of linear regression analysis of all DEG with CGIs in the promoter region; including the proportion of significant negative and positive coefficients over age for both up- and downregulated genes. In this overview, we observe the same general pattern as for the subset of the highly differentially expressed genes (n = 50). There is no correlation between the gene expression level and the methylation status within the upregulated genes.

Coefficient	Upregulated Genes (n = 508)	Downregulated Genes (n = 637)
Positive	82.09%	86.81%
Negative	17.91%	13.19%

Comparison of the mean methylation status (CpGs) within different promoter regions

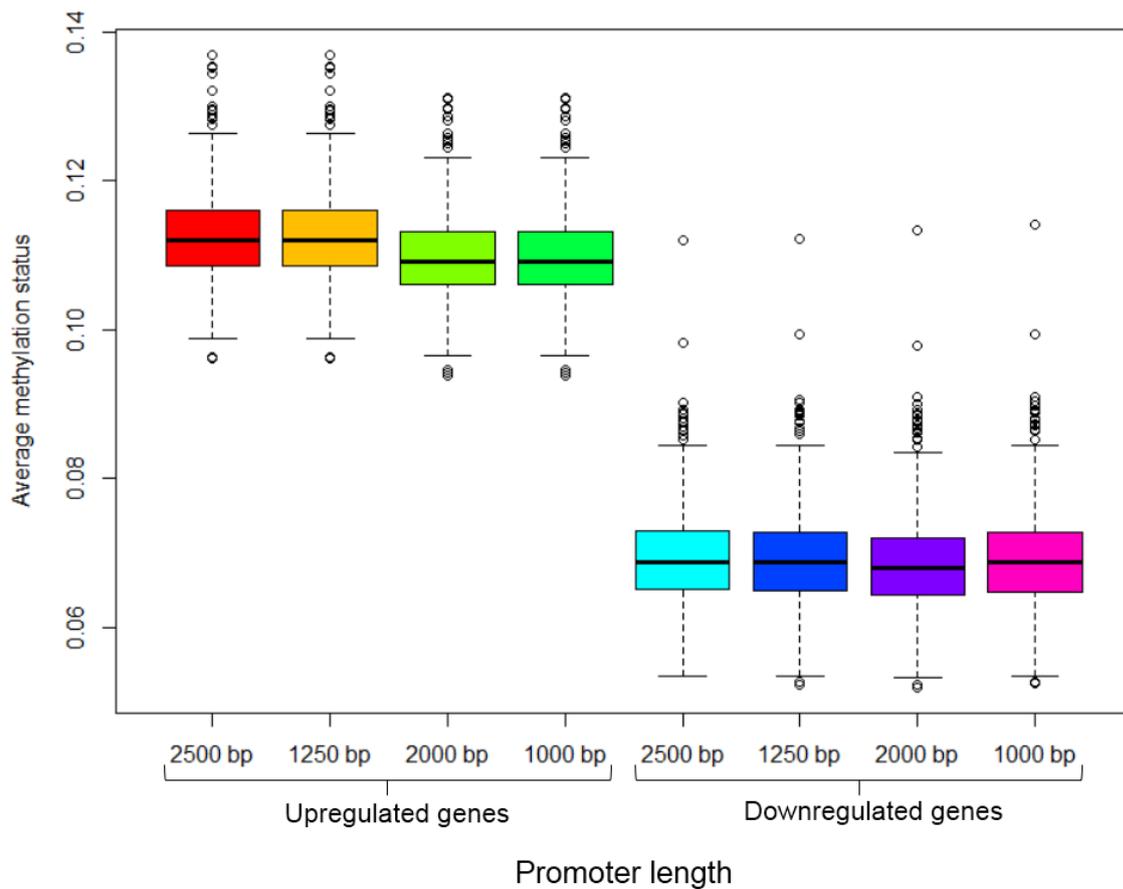


Figure S1: Distributions of the average methylation status of the 25 up- and 25 downregulated genes in promoter regions of varying length. The different regions are: 2 kbp up- and 500 bp downstream, 1 kbp up- and 250 bp downstream, 2 kbp upstream, and 1 kbp upstream. No strong difference between the distributions of the different regions of the downregulated genes is found. The boxplots of the upregulated genes show a small difference between the regions with a downstream part and the regions without downstream sequence.